Sleep and fruit and vegetable consumption in UK adults

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Intellectual Property and Publication Statements

The candidate confirms that the work submitted is her own, except where work which has formed part of jointly authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

Chapter 1 incorporates the work of one jointly authored publication:

Noorwali E, Hardie L, Cade J. Bridging the reciprocal gap between sleep and fruit and vegetable consumption: a review of the evidence, potential mechanisms, implications, and directions for future work. *Nutrients*. 2019,**11** (6), pp.1382.

The candidate was responsible for reviewing the literature and writing all drafts of the manuscript. The contribution of the other authors was providing comprehensive feedback throughout preparation of the publication.

Chapter 2 incorporates the work of one jointly authored publication:

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The candidate contributed to the vitamin C biomarker laboratory analysis. The contribution of the other authors was as follows: Nisreen Alwan helped design the study. Janet Cade conceived the project, oversaw the project, contributed to study design, and helped develop myfood24. Michelle Carter managed the project in Leeds for two years and helped develop myfood24. Paul Elliott helped design the study. Heather Ford led participant recruitment and collection of biological samples. Gary Frost helped design the study and oversaw the participant recruitment process. Darren Greenwood helped design the study and completed the statistical analyses. Neil Hancock contributed to the study design, helped develop myfood24, and continues to manage the myfood24 database. Laura Hardie helped design the study and developed the biomarker methods. Michelle Morris contributed to management of the project in Leeds for one year and helped develop myfood24. Umme Mulla and Katerina Petropoulou managed the project in London, also helping with participant recruitment and biological sample collection.

Greg Potter was responsible for completing the urinary nitrogen and sugars laboratory analyses. David did the plasma β-carotene, α-tocopherol laboratory analyses. Elio Riboli helped design the study. Petra Wark jointly conceived the project, oversaw the project in London, and helped design the study.

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Chapter 5 is the publication:

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The abstract is based on secondary analyses of myfood24 validation data. The candidate contributed to the vitamin C biomarker laboratory analysis. The candidate was not involved in the design, data collection, or primary data processing of myfood24 validation data. Credit for these data is detailed in the publication for Chapter 2. The candidate was responsible for data cleaning and formatting, data interpretation and writing the abstract. Gregory Potter scored sleep records from actimetric data. The contribution of the other authors was providing feedback for the abstract.

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Noorwali EA, Hardie LJ, Burley VJ, Cade JE. Cross-sectional and prospective associations between sleep duration and fruit/vegetable intakes in middle-aged UK women. *Proceedings of the Nutrition Society*. 2018, **77** (OCE4), pp. E131.

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As shown above, several publications have been attained therefore, this thesis will be presented using the thesis by publication format. The incorporation of published papers will inevitably lead to overlapping with other sections in the thesis. The thesis will be constructed by including a literature review (Chapter 1), four chapters of results (chapters 2-5) and the final chapter will include an overall discussion and conclusion (Chapter 6).

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Abstract

A substantial burden of disease globally is attributable to both sleep disruption and low intakes of fruit and vegetable (FV) and increasing mechanistic and epidemiological evidence support a reciprocal relationship between the two. Short and long sleep durations are associated with an increased risk of mortality, diabetes, hypertension, cardiovascular disease and obesity. These associations may be partly mediated by changes in dietary intake including FV consumption. In 2017, an estimated 3.9 million deaths worldwide were attributable to inadequate FV consumption. However, few researchers have explored associations between sleep and FV consumption.

I first explored the cross-sectional associations between objective sleep measures (sleep onset, sleep offset, mid-sleep time and sleep duration) and FV consumption in healthy UK adults. I analysed a biomarker of FV consumption, vitamin C. Subsequent analyses showed that every hour later mid-sleep time (chronotype) was associated with 16% lower intakes of total fruit. Next, prospective analyses of The UK Women's Cohort Study (UKWCS) showed an inverse association between FV intakes and their polyphenol content with sleep duration. Analyses of a nationally representative database showed that sleep duration was non-linearly associated with FV intakes. Short and long sleepers had lower FV intakes compared to the reference group. Finally, using the UKWCS, I explored both cross-sectional and prospective associations between sleep duration and FV consumption. Consistent with the previous findings, sleep duration was non-linearly associated with FV consumption with those sleeping the recommend 7-9 hours/day having the highest intakes compared to short and long sleepers.

This project helped in bridging the gap between sleep duration and FV consumption in UK adults that might have key public health implications. The findings also strengthen the notion that sleep duration and FV consumption have a reciprocal relationship. Finally, this project shows that sleeping the recommended hours is associated with higher intakes of FV.

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List of abbreviations

BMAL1	Brain and muscle aryl hydrocarbon receptor nuclear translocator-like 1
BMI	Body mass index
CCG	Clock-controlled gene
CI	Confidence interval
CLOCK	Circadian locomotor output cycles kaput
CRY	Cryptochrome
DANTE	Diet and Nutrition Tool for Evaluation
DLMO	Dim-light melatonin onset
FFQ	Food frequency questionnaire
FV	Fruits and vegetables
GABA	γ-aminobutyric acid
GI	Glycaemic index
GSPEs	Grape seed proanthocyanidins extracts
HC	High-carbohydrate
HF	High-fat
HPLC	High performance liquid chromatography
KNHNES	Korean National Health and Nutrition Examination Survey
LC	Low-carbohydrate
LCNAAs	Large chain neutral amino acids
LD	Light/dark
LF	Low-fat
LS	Long sleepers
MCTQ	Munich ChronoType Questionnaire
MEQ	Morningness-Eveningness Questionnaire
myfood24	measure your food on one day 24-hour recall
NDNS	National Diet and Nutrition Survey
NHANES	National Health and Nutrition Examination Survey

NREM	Non-rapid eye-movement
NSP	Non-starch polysaccharide
NSF	National Sleep Foundation
NS-SEC	National Statistics-Socio-Economic Classification
OR	Odds ratio
p value	Probability value
PER	Period
Process C	Circadian process
Process S	Sleep process
PSQI	Pittsburgh Sleep Quality Index
REM	Rapid eye-movement
REV-ERB	Reverse-erythroblastosis
ROR	RAR-related orphan receptor
RR	Risk ratio
RS	Reference sleepers
SCN	Suprachiasmatic nuclei
SIRT1	Silent mating type information regulation 2 homolog 1 (SIRTUIN)
SOL	Sleep onset latency
SS	Short sleepers
SWS	Slow-wave sleep
UK	United Kingdom
UKWCS	UK Women's Cohort Study
US	United States
WHO	World Health Organization

Chapter 1: Literature review

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1.1 Prevalence and burdensome of sleep disruption and low intakes of fruits and vegetables

Sleep is a universal need and humans spend about one-third of their lives asleep but its function remains to be fully elucidated. Sleep disruption defined as changes in sleep continuity, timing or duration, is intertwined with circadian rhythm disruption and their causes can be environmental, such as shift work and jetlag, and behavioural, such as the disruption of the fasting/feeding cycle and the rest/activity cycle (1).

The National Sleep Foundation (NSF) (a US non-profit organization) recommends different sleep durations for individuals according to age (Table 1.1.). The NSF conducted a systematic literature review comprised of a multidisciplinary 18-member expert panel including sleep, medicine physiology and science areas. The review focused on medical and scientific research regarding 1) sleep duration data, 2) effects of reduced or prolonged sleep duration, and 3) health consequences of too much or too little sleep. The NSF guidance is based on the health and well-being accompanied with the hours proposed. It included recommended hours (i.e., those hours that experts agree are appropriate for health and well-being), possibly acceptable hours (i.e., those hours that may be appropriate for some individuals), and not recommended hours (i.e., those hours that experts agree are not likely conducive for health and well-being).

Table 1.1. Recommended sleep durations.

Age	Recommended sleep (hours/day)	May be appropriate, (hours/day)	Not recommended (hours/day)
0-3 months	14 to 17	11 to 13 18 to 19	<11 >19
4-11 months	12 to 15	10 to 11 16 to 18	<10 >18
1-2 years	11 to 14	9 to 10 15 to 16	<9 >16
3-5 years	10 to 13	8 to 9 14	<8 >14
6-13 years	9 to 11	7 to 8 12	<7 >12
14-17 years	8 to 10	7 11	<6 >11
18-25 years	7 to 9	6 10 to 11	<6 >10
26-64 years	7 to 9	6 10	<6 >10
≥ 65 years	7 to 8	5 to 6 9	<5 >9

Obtained from The National Sleep Foundation (2).

These recommendations are for healthy individuals not suffering from a sleep disorder with normal sleep. Importantly, it emphasizes that some individuals might sleep longer or shorter than the recommended times with no adverse effects. However, individuals sleeping far outside the normal range may be engaging in voluntary sleep restriction or have serious health problems (2) therefore in this thesis sleep disruption and short/long sleep durations will be used alternatively. The Centers for Disease Control and Prevention has declared “insufficient sleep” as a public health problem because it is associated with type 2 diabetes, heart disease, obesity and depression (3).

A systematic review investigated the secular trends in adult sleep duration over the past 40 years and included 12 studies from 15 countries from the 1960s until the 2000s (4). The authors reported that subjective sleep duration of adults had increased negligibly in Bulgaria, Poland, Canada, France, Britain, Korea and the Netherlands (range: 0.1-0.6 minutes per night each year). Sleep duration decreased in Japan, Russia, Finland, Germany, Belgium and Austria (range:0.1-0.6 minutes per night each year) and inconsistent results were found for the United States and Sweden (4). To gain a better understanding of trends in adult sleep duration, 10 nationally representative data from developed countries were analysed. Short sleep (≤ 6 hours) had increased only in Italy and Norway but had decreased in Sweden, the United Kingdom, and the United States. Long sleep (> 9 hours) had increased in Australia, Finland, Sweden, the United Kingdom, and the United States but had decreased in Canada and Italy. No changes were observed in Germany or the Netherlands (5). A recent meta-analysis of healthy adults found no reduction in objective sleep duration over the last 50+ years (6). However, adults were not representative of the adult population at large. Findings of several countries since the 1990s suggest a decline in subjective sleep quality in the adult population (7). The previous studies provide mixed results in the stability of sleep duration and quality and more studies using objective measures of sleep at a population level are needed to confirm that sleep duration and quality has deteriorated over time (8).

The Sleep Council in 2010 reported that 27% of UK adults slept for just five to-six hours per night. In 2013, in a survey of 5007 UK adults, they reported that 70% of UK adults slept for 7 hours or less per night and 27% experienced poor sleep quality on a regular basis (9). In 2017, The Sleep Council reported that UK adults are sleeping less than 2013, with 74% sleeping less than 7 hours per night and 30% reporting poor sleep quality (10). In 2013 and 2017, the main reasons for disrupted sleep were stress and worry, partner disturbance, noise and an uncomfortable bed (9, 10). In a representative cohort

of ~124,000 US adults, paid work time was the primary waking activity exchanged for sleep (11).

A recent meta-analysis reported on the prevalence of poor sleep quality and sleep duration in low and middle-income countries (12). The findings from 20 studies suggest that approximately one third of the adult population (n=231,542 individuals) in low and middle income countries report disturbed sleep duration and quality. However, more research is needed in less-developed countries.

Hafner and colleagues reported the economic cost of insufficient sleep from 62,000 people in the UK, US, Canada, Germany and Japan. Insufficient sleep costs $411 billion annually for the US, $138 billion for Japan, £40 billion for UK, $60 billion for Germany and $21 billion for Canada (13). Sleep disruption has detrimental consequences (see section 1.2.1) and identifying the factors that influence it is a public health priority.

A reciprocal relationship appears to exist between sleep and dietary intake, sleep disruption affects dietary intake (discussed in section 1.5.1) and dietary intake affects sleep (discussed in section 1.5.3). With this reciprocal relationship in mind, The World Health Organization (WHO) recommends consuming 400 grams or more of FV per day to improve overall health and reduce the risk of chronic diseases (14). The recommended amount of FV consumption is different between countries, The US Department of agriculture recommends FV based on age, sex, and level of physical activity. Using “My Plate” they recommend Americans to fill half their plates with FV for meals (15). The Australian Guide to Healthy Eating recommends 2-8 servings of vegetables and 1-5 servings of fruit per day (16), Canada’s Food Guide recommends consuming 4-10 servings of FV depending on age and sex (17). The Food-based dietary guidelines for Denmark recommends eating at least 600 grams/day of FV for a healthy population aged over 3 years (18) and the UK Eatwell Guide recommends consuming at least 5 portions of FV per day (19).

Despite these recommendations, FV consumption remain below the recommended levels and below the WHO recommendations in many countries (14, 20, 21). In 2014, only 30% of UK adults aged 19-64 years and 41% of adults aged ≥65 years consumed 5 portions of FV per day according to Public Health England (22). In 2016, 25% of UK men and 28% of women aged 19-64 years met the 5-A-Day recommendation of FV consumption (23). In 2019, the trends in population intakes for all UK participants were presented. Over the 9-year period of the UK National Diet and Nutrition Survey (NDNS), minor changes were observed for total FV consumption in adults aged 19-64 years. There was an annual increase of an average of 5 grams/day of total FV observed in men

aged 19-64 years. In respect to meeting the 5-A-Day recommendations for FV intakes, negligible changes were observed over the 9-year period and all age/sex groups had a mean FV intake below the 5-A-Day recommendation (24).

Few studies have assessed the economic cost of "unhealthy diets" that includes low consumption of FV, probably due to the conceptual challenges of its definition (25). Popkin et al. defined an "unhealthy diet" as high in saturated and trans-fat, heavy alcohol drinking, and low consumption of whole grains and FV. Using this definition, the estimated annual cost of "unhealthy diets" for China was calculated as €3.5 billion per capita (26). The economic burden attributable to low FV consumption in Australia was estimated to be $AUS 269 million (27). For Canada, the economic burden of inadequate consumption of FV was $CAN 3.3 billion per year, of which 30% is directly associated with health-care costs and 69% is indirect costs due to productivity losses (28). The estimates of the economic cost to the NHS in the UK in 2007 was £5.8 billion for "poor diet", the consumption of <600 grams/day of FV was one aspect of "poor diet" (29).

It is clear that sleep disruption and low consumption of FV are both economically burdensome but their detrimental health consequences are increasingly evident (see section 1.2.1).

1.2 Sleep disruption and low intakes of fruit and vegetable are associated with morbidity and mortality

1.2.1 Sleep disruption, morbidity and mortality

There is growing evidence that sleep disruption has deleterious associations for health. Several meta-analyses in children and adolescents found that short sleep duration was associated with higher risks of overweight and obesity (30-33). The most recent meta-analysis from fifty prospective cohorts including 35,540 children and adolescents from around the world showed that short sleep duration had a 71% higher risk of obesity (Odds ratio (OR) 1.71 95% CI 1.36 to 2.14) (34). Similarly, subjective poor sleep quality (independent of sleep duration) was associated with higher odds of being overweight and obese (35). However, the latter study included participants between <2 - 34 years and as sleep quality declines with age (36), future studies considering different age ranges are crucial.

With respect to adults, short sleep duration was associated with a 45% increased risk of obesity in adults from a meta-analysis of prospective studies (37). This was consistent with the most recent meta-analysis including 5,172,710 participants from 153 prospective studies. Short sleep duration was associated with 38% (Risk ratios (RR) 1.38 95% CI 1.25 to 1.53) increased risk of obesity (38). Recent evidence from other meta-

analyses found that long sleep duration is also associated with increased risk of obesity (39, 40). Sleep disruption was shown to increase the risk of other diseases including; cancer (41-43), type 2 diabetes mellitus (38, 39, 44), stroke (45), cardiovascular disease and coronary heart disease (46, 47).

Several studies assessed the association between sleep disruption and mortality. A consistent U-shaped association was shown between sleep duration and mortality, short and long sleep durations were associated with an increased risk of mortality (38, 39, 48-51). In the most recent meta-analysis, short sleep duration (RR=1.12 95% CI 1.08 to 1.16) (38) and long sleep (RR=1.39 95% CI 1.31 to1.47) (39) were associated with an increased risk of mortality. Collectively, sleep disruption is associated with an increased risk of diseases and mortality. These associations may be partly mediated through changes in dietary intake including the low consumption of FV (52), thus exploring the associations between sleep and dietary intake is fundamental.

1.2.2 Low intakes of fruit and vegetable, morbidity and mortality

Increased consumption of FV has been shown to protect against type 2 diabetes (53), coronary heart disease (54), stroke (55) and some cancers (56). Increasing FV consumption to 600 grams/day could reduce the total worldwide burden of disease by 1.8%, reduce the burden of ischemic heart disease by 31%, ischemic stroke by 19%, stomach cancer by 19%, esophageal cancer by 20%, lung cancer by 12% and colorectal cancer by 2% (57). Recent evidence from a dose-response meta-analysis of prospective studies suggests that the consumption of 800 grams per day (10 portions per day) of FV is associated with lower risks of cardiovascular diseases, cancer and all-cause mortality (58).

A substantial burden of premature deaths globally is attributable to low consumption of FV. In 2005, total worldwide mortality attributable to inadequate consumption of FV is estimated to be up to 2.635 million deaths per year (57). In 2013, an estimated 5.6 million premature deaths worldwide may be attributable to FV intakes below 500 grams per day and 7.8 million premature deaths to FV intakes below 800 grams per day (58). In 2017, an estimated 3.9 million deaths worldwide were attributable to inadequate FV consumption according to WHO (59). These studies highlight the importance of FV consumption thus, identifying lifestyle factors, which may influence FV intakes, is a public health priority.

Biomarkers such as plasma vitamin C and serum carotenoids (lutein, zeaxanthin, β-cryptoxanthin, α- and β-carotene and lycopene), are well established biomarkers of FV consumption (60). Dietary intakes and blood concentrations of vitamin C and carotenoids

were inversely associated with coronary heart disease, cardiovascular disease, stroke, cancer and all-cause mortality from a recent dose-response meta-analysis from 66 prospective studies (61).

The previous studies showed that sleep disruption, low intakes of FV and low levels of FV biomarkers are attributable factors to morbidity and mortality consequently, bridging the scientific gap between their associations is essential and may have key public health implications.

1.3 Sleep

1.3.1 Sleep architecture and assessment

Normal sleep architecture comprises non-rapid eye-movement (NREM) sleep and rapid eye-movement (REM) sleep which alternate cyclically over the course of a period of sleep (62). NREM sleep is further divided to stages 1, 2, 3, and 4. Stages 3 and 4 combined provide slow-wave sleep (SWS) (63). These sleep cycles and stages were identified with the use of electroencephalogram (64, 65) or polysomnography which is considered the gold standard for sleep assessment (66). Sleep begins with NREM stage 1 progressing to stage 2, 3 and 4 and finally to REM, and the cycle between these stages continue throughout the night. NREM sleep constitutes about 75-80% of total sleep time whereas REM sleep constitutes the remaining 20-25% (62). The polysomnography can determine the sleep stage of the participant at any time and the transitions occurring between the states. In addition, the polysomnography produce more information such as oxygen saturations, limb movements, apnoea's, respiratory events, heart rate, core body temperature etc. that can be used to diagnose sleep diseases (67).

Another objective method of sleep assessment is actigraphy, which is a non-invasive and less expensive method. Actigraphy collects activity information over a period of time and has the advantage of providing objective information on sleep in the participants' natural sleep environment (68). Actigraphy was validated against polysomnography and showed reliable measures of sleep duration in patients with schizophrenia or bipolar disorder (69) and in healthy adults (70).

Besides sleep architecture, sleep health encompasses multiple dimensions of sleep (Table 1.2.). These include sleep duration, quality (efficiency which is the time in bed spent asleep, sleep onset latency (SOL) which is the amount of time it takes to fall asleep) (71), timing (sleep onset is the time sleeping starts and sleep offset is waking time), variability, daytime sleepiness and napping (72). However, most studies have focused on sleep duration since it is easier to report accurately by participants (39). In addition, sleep duration and sleep quality are inextricably linked, people with short and

long sleep durations are the most likely to report sleep disturbances (73, 74). It has been suggested that the extremes of sleep duration (short/long) capture poor sleep quality and that poor sleep quality may partly explain the U-shaped associations observed between sleep duration, morbidity and mortality (75) (see section 1.2.1). Chronotype has been defined as "*An individual's phase angle of entrainment (for example, the timing of core body temperature nadir relative to dawn)"*(1) which is the preference in timing of activity and sleep referred to as morning or evening type (76). Chronotype has been assessed by various methods such as the Horne and Östberg's Morningness-Eveningness Questionnaire (MEQ)(77). However, the main limitation of MEQ is the unavailability of sleep timing estimates. This has been developed to the Munich ChronoType Questionnaire (MCTQ)(76) that uses mid-sleep time on non-work days as an estimate of chronotype after correcting for sleep debt on work days. In this thesis, I will refer to chronotype when discussing studies that used any method of chronotype assessment.

Table 1.2. Sleep measures glossary

Sleep timing	
Sleep onset	The time sleeping starts
Sleep offset	Waking time
Sleep quality	*"Sleep quality is defined as one's satisfaction of the sleep experience, integrating aspects of sleep initiation, sleep maintenance, sleep quantity, and refreshment upon awakening" (78)*
Sleep efficiency	Total sleep duration/total time spent in bed X 100 (71)
Sleep onset latency (SOL)	The amount of time it takes to fall asleep
Sleep duration	*"The total amount of sleep obtained, either during the nocturnal sleep episode or across the 24-h period"(78)*
Sleep disruption	*"Externally mediated changes in sleep continuity, timing, or duration (restriction entails reduced sleep duration, whereas deprivation is the absence of sleep)"(1)*
Chronotype	*An individual's phase angle of entrainment (for example, the timing of core body temperature nadir relative to dawn)"*(1)

Sleep questionnaires for detecting sleep disorders are numerous including Mini sleep Questionnaire, Epworth Sleepiness Scale, Insomnia Severity Index, Sleep Disorders Questionnaire, Sleep Apnoea clinical score and others that have been previously reviewed (67). However, The Pittsburgh Sleep Quality Inventory (PSQI) questionnaire that measures sleep quality and patterns of sleep in adults has been widely used in many studies. The PSQI is a subjective measure that assesses seven factors of sleep; sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. A global sleep score is created by totalling the seven factor scores, with higher scores indicating poorer sleep quality. The PSQI showed a high degree of internal homogeneity, meaning each of the seven components measured a particular aspect of the same overall construct (sleep quality) and reliability. Validity of the PSQI with polysomnography showed no differences in SOL but PSQI estimates of sleep duration and efficiency were greater than those obtained from polysomnography (79).

A recent systematic review compared between sleep questionnaires and diaries and reviewed their validation (80). Sleep diaries have an advantage over sleep questionnaires, they are filled over a period of time (usually one or two weeks) whereas sleep questionnaires are filled in once. In addition, sleep diaries collect information everyday accounting for variability whereas sleep questionnaires collect information based on memory about the previous one or two weeks. Modern sleep diaries come in the form of an app and have several advantages in comparison to paper sleep diaries such as automatic recording of the time when the diary was filled and automatic scoring that reduces the time for data entry (80). Two studies compared between the accuracy of electronic and paper sleep diaries (81, 82) and both studies concluded that electronic sleep diaries perform like paper sleep diaries and if future studies confirmed this in clinical populations, then electronic sleep diaries should replace paper sleep diaries.

In regard to the comparison between subjective report of sleep duration and objective measures, conflicting results have been shown. In a validation study of 56 Australian women, poor agreement were shown between actigraphy data and subjective reports of sleep duration, efficiency sleep quality and SOL. Participants tended to underestimate their sleep duration compared with objective measures (83). In contrast self-report of sleep duration in 669 young adults was overestimated compared to actigraphy measures (84). This was consistent in a more recent study including 35 healthy adults (81), self-report of sleep duration was overestimated compared to actigraphy measures however, a positive significant correlation was shown with paper sleep diary (Pearson's r= 0.39, $p<0.05$) and electronic sleep diary (Pearson's r= 0.64, $p<0.01$). Similarly, sleep duration

was overestimated by 26 minutes using an electronic sleep diary and 27 minutes using a paper sleep diary in 15 healthy adults in comparison to actigraphy (82). The different results may be due to the different sample sizes and the length of sleep assessment however, participants mostly overestimated self-report of sleep duration in comparison with objective methods.

Overall, all sleep assessment methods have advantages and disadvantages and therefore, objective measures of sleep should be combined with sleep diaries to provide accurate measures of sleep.

1.3.2 Regulation of sleep/wake cycle

In 1982, Borbély proposed a two-process model that interplay to regulate sleep akin to an hourglass timer (85).The two-processes include process S which is the homeostatic drive to sleep which accumulates across the day, peaks before bedtime and dissipates throughout the night. On the other hand, process C promotes wakefulness and is regulated by the circadian system. Process C counteracts process S across the day and declines at bedtime (62).

Sleep process S is regulated by sleep/wake generating systems in the brain stem. Neurons that are found in the hypothalamus in the brainstem shut down the arousal systems allowing the brain to sleep. Wakefulness happens by two pathways in the upper brainstem causing ascending arousal which originate in cholinergic neurons and cell groups. The cholinergic neurons activate parts of the thalamus that maintain transmission of sensory information to the cerebral cortex. In the upper brainstem, the cell groups contain neurotransmitters (norepinephrine, serotonin, dopamine and histamine) that enter the hypothalamus, pick up inputs from nerve cells, enter the cerebral cortex and activate the nerve cells preparing them for incoming sensory information (62). Dietary neurotransmitters are available in different foods including FV that participate in essential metabolic processes which influence sleep however, their significance need to be further investigated (86).

The planet rotates around its axis which results in the 24-hour cycle of light and darkness. All life forms from cyanobacteria to human beings adapt to the light/dark (LD) cycle with endogenous circadian rhythms that are entrainable in ~24 hours (87). The suprachiasmatic nuclei (SCN) in the anterior hypothalamus regulates the circadian rhythms in all body organs (88). The LD cycle is the primary zeitgeber -"*the oscillation force that entrains the biological rhythm"* (1)- for humans. Light is detected by intrinsically photosensitive retinal ganglion cells in the inner retinae, primarily entraining the SCN. In response to light stimuli, the SCN controls the synthesis of melatonin, a hormone

produced by the pineal gland, which increases sleep propensity and contribute to synchronisation of circadian rhythms in other tissues (88). The SCN then synchronise all circadian rhythms in other tissues with the external LD cycle (1).

This synchronisation is regulated by clock genes that also exist in cells throughout bodily tissues. These clock genes form negative-feedback loops to maintain activity and rest phases. During the rest phase, the transcription factor proteins circadian locomotor output cycles kaput (CLOCK) and brain and muscle aryl hydrocarbon receptor nuclear translocator-like 1 (BMAL1) bind together and activate clock controlled genes (CCG). In response, the proteins cryptochrome (CRY 1-2) and period (PER) 1-3 accumulate in the cytosol. They then move back to the nucleus and inhibit CLOCK-BMAL1. As the rest phase progresses to the activity phase, PER-CRY proteins are degraded and CLOCK-BMAL1 are activated. Furthermore, BMAL1 transcription is regulated by two nuclear receptors; reverse-erythroblastosis (REV-ERB) α and β repress BMAL1 transcription, whereas RAR-related orphan receptor (ROR) α activates BMAL1 transcription (88). Accordingly, the activation and deactivation of PER-CRY proteins is the basis of the negative-feedback loop and their ability to modulate their own production allows the system to self-regulate and thus process C interact with process S to regulate sleep/wake cycles.

Another mechanism by which the SCN contribute to sleep is by regulating the circadian rhythm of body temperature. Sleep onset is promoted and maintained by an individual's body temperature. During the day, body temperature is higher than at night, then at night there is an increase in heat loss and a decline in body temperature. Conversely, several hours before waking up, body temperature gradually increases and heat production increases in other body parts disrupting sleep and promoting wakefulness (62).

1.4 Fruits and vegetables

FV are a group of plant foods that vary considerably in their content of energy and nutrients. FV contain fibers, vitamins, minerals, and polyphenols that function as antioxidants (89), this thesis will focus on only polyphenol effects on sleep.

In a systematic review exploring the environmental determinants of FV consumption among adults; household income, marital status, having children and local availability influenced the intake of FV (90). Adults with lower household incomes had lower intakes of FV whereas married people had higher intakes compared to those who were single and having children showed mixed results. Furthermore, having low food insecurity and having access and availability of FV exerted positive influence on FV consumption in adults. Another systematic review identified the psychosocial determinants of FV

consumption in adults from 23 studies. The most consistent predictors of FV consumption were habit, motivation and goals, beliefs about capabilities, knowledge and taste. Intentional predictors included beliefs about capabilities, beliefs about consequences and perceived social influences (91).

Factors affecting FV choice are complex and include sensory appeal, familiarity and habit, social interactions, cost, availability, time constraints, personal ideology, media advertising and health (92). Health is influenced by sleep disruption and thus identifying if sleep disruption is associated with FV consumption is necessary.

1.5 The reciprocal relationship between sleep and dietary intake

The reciprocal relationship between sleep and diet in humans has been studied since the 1980s (93-95). Hicks et al assessed the association between sleep duration and eating disorders using a 26-item Eating Attitude Test in college students. Short sleepers (≤ 6 hours/night, n=34) were five times more likely to exhibit abnormal eating patterns compared to long sleepers (≥ 8 hours/night, n=43) (94). Hicks et al. further studied the relationship between sleep duration and eating behaviours of college students. Short sleepers (n=31) showed a tendency to eat more small meals or snacks than long sleepers (n=37) who were satisfied with their sleep (95). Analyses including 3,790 women indicated that women who reported insufficient sleep, poor sleep, problems falling asleep and disturbed sleep had higher odds of binge eating (96). The association between unfavourable dietary behaviours including; dinner within 2 hours before sleep more than 3 days a week, snacking after dinner, eating rapidly, skipping breakfast and sleep duration was studied in 9,643 Japanese adults (97). Results showed that an increase in the number of unfavourable dietary behaviours was associated with shorter sleep.

1.5.1 Sleep affects diet: experimental studies

Several experimental studies observed an increase in food intake after sleep restriction (98). Spiegel et al. reported a 24% increase in hunger and 23% increase in appetite especially for calorie-dense foods with high carbohydrate content after two days of experimental sleep restriction (4 hours) compared to controls (99). In contrast, 50 undergraduate students who were instructed to sleep for 4 hours or less consumed less calories following sleep restriction (100) however, the study did not include a control group. Sleep restricted to 5.5 hours for 14 days in healthy participants with ad libitum access to palatable food was accompanied by increased consumption of energy from snacks with no change in energy from meals compared to sleeping 8.5 hours (101).

Brondel et al. observed a significant increase in energy intake, pre-prandial hunger before breakfast and dinner and higher fat intake after one night of sleep restriction to 4 hours in twelve healthy men in comparison to those who slept 8 hours (102). Five hours of sleep for 5 days in 16 adults resulted in small portions of breakfast but larger portions throughout the day specifically after dinner (103). Furthermore, after one night of sleep deprivation compared to 8 hours of sleep, participants selected larger portions irrespective of the type of food (104). After 5 nights of sleep restriction to 4 hours in 37 healthy adults compared to controls who spent 10 hours in bed, sleep restricted participants consumed more calories due to more meals and the increased consumption of calories were derived from fat during late-night hours (105). After one night of sleep restriction, participants experienced decreased alertness and preference for energy-dense foods more than healthy food choices (106).

A meta-analysis conducted by Capers et al aimed to assess the association between interventional studies of sleep disruption and measures of body composition, energy expenditure and food intake (107). Eighteen studies were included and the results showed that studies restricting sleep indicated weight gain or less weight loss compared to controls. Studies increasing sleep duration revealed inconsistent results on body weight. Studies of sleep disruption indicated a non-significant increase in total energy expenditure with high heterogeneity. Studies assessing the effects of sleep restriction on food intake were not included in the meta-analysis and were instead narratively summarized in the results and suggested that sleep restriction from interventional studies increases food intake. A recent meta-analysis assessed the effects of sleep restriction from human intervention studies on energy intake and energy expenditure (108). Seventeen studies with 496 participants were included in the systematic review and 11 studies (n=172 participants) were included in the meta-analysis. Energy intake was increased by 385 kcal (95% CI 252 to 517) following sleep restriction (not standardised between studies) compared with controls accompanied by higher fat and lower protein intakes and no effect on carbohydrate intakes. Total energy expenditure and resting metabolic rate was not changed in response to sleep restriction.

In summary, the previous studies indicate an increase in energy intake following sleep restriction and deprivation in experimental settings. However, the generalizability of the results may be limited due to the controlled conditions. They may be addressed by exploring the relationships between sleep restriction, deprivation and diet using large cohorts from real life.

1.5.2 Sleep and diet: observational studies

Cross-sectional research methods are beneficial in understanding associations between sleep and diet. They can be used to identify population trends and also highlight valuable research questions to pursue in more controlled settings. The limitation of cross-sectional studies is that causal relationships cannot be inferred, and the use of a range of assessment tools and analytic methods in different populations often results in conflicting results between nutritional epidemiology studies. Cross-sectional studies have therefore produced insights into the associations between sleep and diet in many locations worldwide, but there have sometimes been contradictory findings regarding how sleep disruption relates to dietary intake. Prospective studies have higher accuracy and there is a need for more prospective studies to assess the associations between sleep and diet. The potential mechanisms of how sleep disruption affects dietary intake have been reviewed previously (Figure 1.1.) (52).

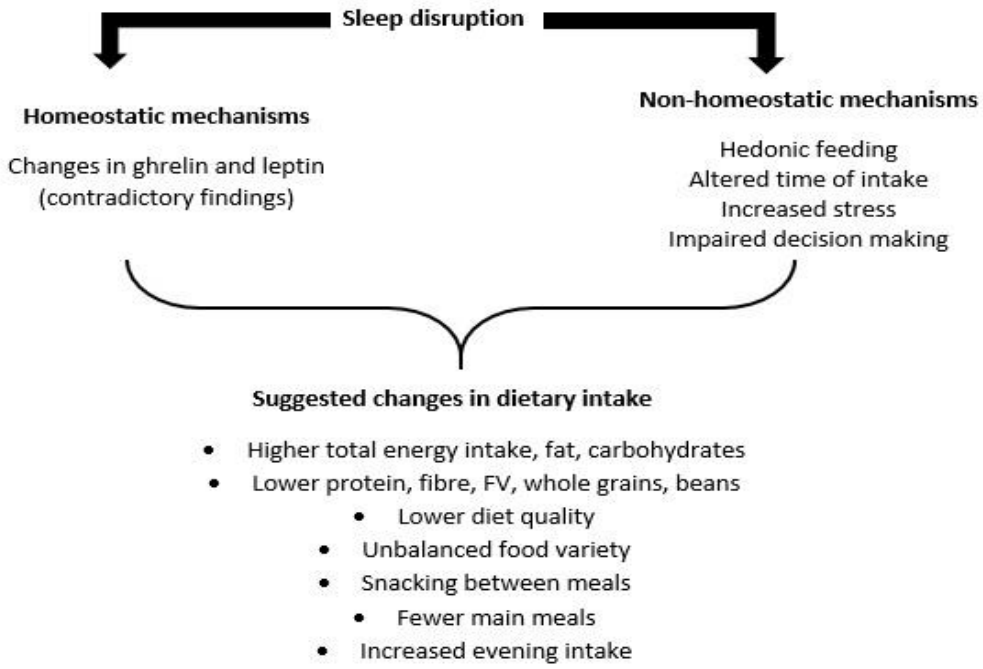

Figure 1.1. Mechanisms for the effects of sleep disruption on dietary intake.

Sleep disruption affects dietary intake through homeostatic and non-homeostatic mechanisms therefore, in this thesis, chapters 2, 4 and 5 used sleep duration as the exposure. Adapted from (52).

FV (fruits and vegetables)

1.5.2.1 Macronutrients

Shi et al assessed the reciprocal association between sleep duration and fat intake in 2828 Chinese adults from a National Survey of Nutrition and Health. Adults sleeping <7 hours per day had higher percentage of energy from fat intake than those sleeping 7-9 hours per day. Reversing the analyses, there was a trend of reduced sleep in the highest quartiles of fat intake compared to the lowest (109). Furthermore, cross-sectional analyses of 410 female Iranian students indicated that those sleeping <6 hours consumed more energy and carbohydrates compared to those sleeping >8 hours (110). Using the American National Health and Nutrition Examination Survey (NHANES) including 5587 adults, sleeping <5 hours and ≥ 9 hours were associated with a decreased intake of protein, carbohydrates, sugars, dietary fibre and fat compared to adults sleeping 7-8 hours (111). Similarly, using the NHANES including 15,199 adults, short sleepers (≤ 6 hours) consumed less energy from meals but higher energy from snacks compared to average sleep duration (7-8 hours). In addition, short sleepers had higher total sugar intake however, few differences were observed in macronutrient composition of energy content of the diet between sleep duration groups (112). Consistently, short sleep duration was associated with higher energy intake among US adults (113).

Postmenopausal women who reported sleeping ≤6 and ≥8 hours per night reported higher energy intake and lower diet quality assessed by the Alternate Healthy Eating Index score compared to women sleeping 7 hours per night (114). Similarly, sleep duration was negatively associated with fat intake in 459 post-menopausal women (115). Short sleep duration was associated with higher energy, fat and alcohol intake in 118 obese men and premenopausal women (116). Korean women (n=8,384) from the Korean National Health and Nutrition Examination Survey (KNHNES) sleeping <7 hours per day consumed more dietary carbohydrates compared to those sleeping ≥7 hours per day (117). This was consistent with another analyses using the KNHNES although short sleep duration was defined as ≤6 hours per day (118). Sleep duration was positively associated with protein consumption in both men and women. Men sleeping ≤6 hours per day consumed more fat and women sleeping ≤6 hours per day consumed more carbohydrates compared with participants sleeping 7-8 hours per day. Similarly, Doo et al conducted a cross-sectional analyses to examine the association between sleep duration and the risk of obesity according to dietary macronutrient consumption in 14,680 Korean adults using the KNHNES (119). Participants sleeping ≤5 hours per day consumed less dietary protein and fat and more dietary carbohydrate. Short sleepers with high fat intake had higher odds of obesity risk compared to low fat intake. In contrast, short sleepers with low carbohydrate intake had lower risks of obesity.

In a meta-analysis including 14,906 participants from 9 American and European cohorts, sleep duration was inversely associated with carbohydrate and fat intake (120). Using 7 day actigraphy and sleep diaries in 439 participants, higher sleep fragmentation (interruptions of sleep) was associated with lower carbohydrate intake (121). Australian women sleeping ~8 hours but with sleeping difficulties and severe tiredness were inversely associated with protein intake and women with short sleep ~6 hours with sleeping difficulties and severe tiredness were positively associated with fat intake (122). In contrast, sleep duration was not associated with macronutrient intake in UK adults (n=1615) from the NDNS (123).

A number of observational studies assessed the association between dietary intake and sleep with sleep as the outcome. Dietary intake was measured by a 3 day consecutive food diary before assessing sleep by polysomnography in 52 healthy adults. A negative association was observed between nocturnal fat intakes (fat consumed in the evening period) and sleep efficiency and REM sleep and a positive association between nocturnal fat intake and SOL in men. In women, energy, nocturnal fat, and carbohydrate intakes were positively associated with SOL and REM sleep latency (124). Macronutrient and dietary habits in association with sleep duration and regularity of sleep timing was examined in 1,368 Japanese adults (125). High intakes of carbohydrates and low intakes of protein were associated with irregular sleep. Furthermore, prospective analyses between meal specific macronutrients and sleep duration over 5 years was assessed in 1474 Chinese adults. A high fat breakfast was associated with less falling asleep during the day at follow up. Whereas a high fat dinner was associated with persistent short sleep over 5 years indicating that the association between macronutrient intake and sleep duration differs by the time they were consumed (126).

Together, the previous studies show inconsistent results with sex differences in the association between sleep duration and macronutrients however a positive association was found between sleep duration and energy intake consistent with experimental studies in humans (see section 1.5.1) and animal studies (127). The conflicting results of macronutrient intake in relation to sleep duration may be due to the variations in the definitions of sleep duration, the variations in dietary assessment methods and different populations and age groups.

1.5.2.2 Micronutrients

Several studies have assessed the associations between dietary nutrients and different sleep measures. Later sleep was positively associated with dietary vitamin D and napping was positively associated with fat intake, amino acids and cholesterol in 459 post-menopausal women (115). Furthermore, Grandner et al assessed the associations

between dietary nutrients and sleep duration categories using the NHANES (n=5587) (111). Sleeping <5 hours was associated with lower intakes of lycopene, thiamine, total folate and folic acid. Similarly, sleeping <5 hours and ≥9 hours were associated with lower intakes of minerals including calcium, phosphorus, magnesium, iron, zinc, sodium, potassium and selenium compared to the reference group (7-8 hours) of sleep.

Grandner et al assessed the associations between dietary nutrients and other sleep measures including difficulty falling asleep, sleep maintenance difficulties, non-restorative sleep (defined as the " *subjective feeling that sleep has been insufficiently refreshing, often despite the appearance of physiologically normal sleep* (128)) and sleepiness in 4,552 adults using the NHANES (129). Reduced intakes of several nutrients including alpha-carotene (FV are main sources of carotenoid intake (130)) were associated with difficulty falling asleep. Increased intake of moisture – refers to total moisture content of foods and beverages (e.g. watermelon, lettuce and coffee) - were associated with sleep maintenance difficulties. Decreased intakes of vitamin C was associated with non-restorative sleep. Micronutrient intakes differed between insomniacs and normal sleepers in Indian adults. Insomniacs consumed less thiamine, folic acid, vitamin B_{12} and iron (131).

A recent systematic review was conducted to assess the relationship between micronutrient status and sleep patterns including all age groups that included twenty six studies (132). Iron and magnesium status were shown to be important in the development of sleep stages among infants and in reversing age-related alterations in sleep among older adults. Furthermore, the studies indicated a positive association between sleep duration with iron, zinc and magnesium levels and an inverse association between sleep duration with copper, vitamin K and vitamin B_{12} levels.

The number of studies suggesting a link between micronutrient status and sleep are few indicating a need for more studies. Longitudinal and intervention studies investigating dose and time dependency between micronutrients and various sleep measures across different populations are essential to clarify this relationship. Consequently, examining the clinical relevance of micronutrients on sleep health may help nutritionists, and sleep practitioners.

1.5.3 Diet affects sleep: experimental studies

Several experimental studies assessed the effects of low-carbohydrate (LC), high-carbohydrate (HC), low-fat (LF), high-fat (HF) diets, milk, fruits, fatty fish, herbal products, glycaemic index (GI) of foods, protein and fat on different sleep measures and architecture (71, 133, 134).

1.5.3.1 Macronutrients

In 1975, Phillips et al studied the effects of a HC-LF or LC-HF diet on sleep architecture for 4 days in 8 healthy men (135). Both HC-LF and LC-HF diets were associated with more REM sleep compared to the balanced diet with a greater increase after the consumption of the HC-LF diet whereas SWS decreased with the HC-LF diet. Yajima et al observed a decrease in SWS following a HC diet compared to those who consumed a HF diet however, the study did not provide a control group (136). Another study investigated the effects of different carbohydrate levels with similar protein and fat content with a pre-bedtime meal, administered 45 minutes before sleep, on sleep architecture in men. Intervention included 3 nights of a HC, LC and zero carbohydrate. Following the consumption of the HC diet, NREM sleep decreased and REM periods increased compared to the zero carbohydrate diet. In contrast, REM latency increased after the LC diet in comparison to the HC diet (137).

Kwan et al studied the effects of a LC diet (50 g/d) for 1 week on sleep architecture in 6 healthy women. REM onset latency increased after the LC diet with no changes in sleep time (138). Wells et al assessed the effects of meal composition on daytime sleepiness in 8 men and 8 women (139). Sleepiness was enhanced after the meals however, there was no difference in sleepiness according to the composition of the meal. Furthermore, reduction of SOL was observed after the consumption of a high GI meal 4 hours before bed time compared to low GI meals in 12 healthy men with no difference observed on other sleep measures including sleep duration (140). Afaghi et al compared the effect of LC diet and a controlled mixed diet on sleep architecture in 14 healthy men. LC diet increased the percentage of SWS and reduced the percentage of REM sleep compared to the mixed diet (141). In more recent studies, Lindseth et al studied the effects of macronutrients intake on sleep architecture in 44 adults. Participants consumed a HC, HF, high protein and a control diet for 4 days and subsequently their sleep was measured using actigraph watches. High protein diets were associated with fewer wake episodes and a HC diet was associated with shorter SOL compared with the control diet (142). Similarly, Lindseth observed shorter wake times (after sleep onset) following a HC diet and better sleep assessed by the PSQI after a HF diet compared to a control diet in 34 adults (143).

The previous experimental studies showed that HC and HF diets may modulate sleep architecture but the results are inconsistent and mixed. Macronutrient intakes influenced sleep architecture with limited evidence on sleep duration. Further longitudinal studies are needed to confirm the effects of macronutrient intakes on sleep measures due to the small number of participants and the short term nature of interventions.

1.5.3.1.1 Mechanisms for the relationship between nutrient intakes and sleep

The mechanisms of how nutrients including carbohydrates, fat, protein, vitamins, minerals and probiotics affect sleep measures have been previously reviewed (133) with more promising effects of protein intakes, specifically amino acid tryptophan (144, 145) through modulation of sleep-wake promoting neurochemicals (146, 147). The main pathways of how nutrients promote sleep-wake are through the gastrointestinal tract, precursors for serotonin and melatonin, bioactive molecules and other unidentified mechanisms (Figure 1.2.).

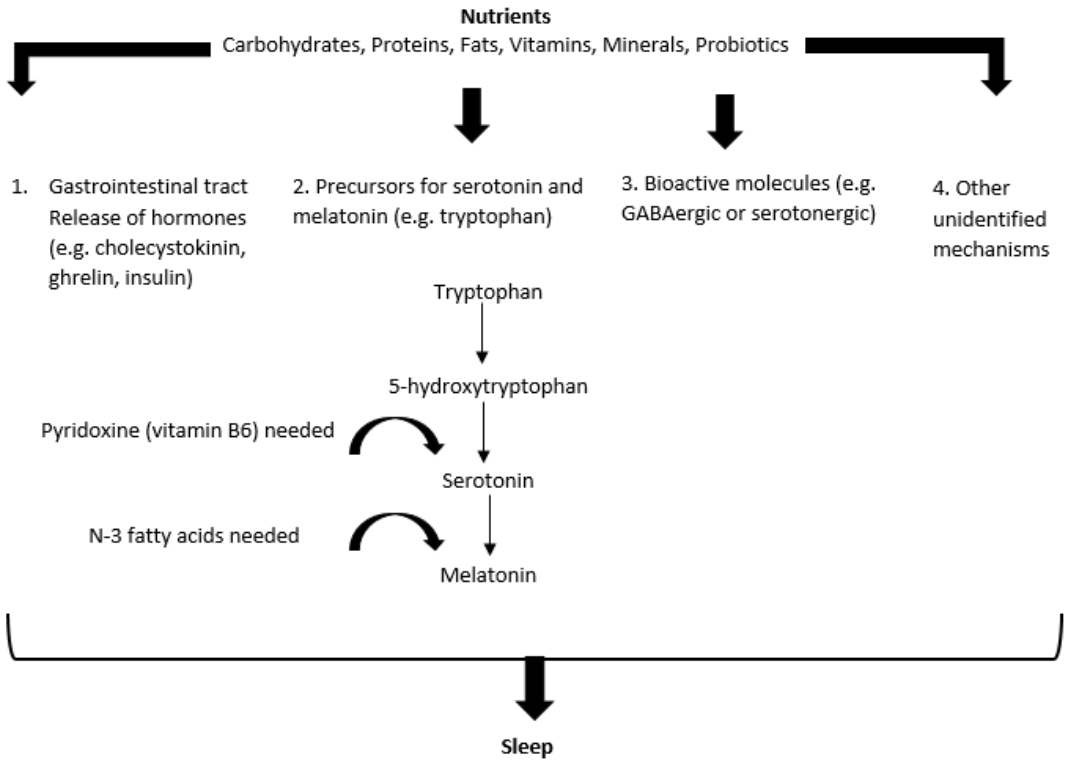

Figure 1.2. Mechanisms for the effects of diet on sleep

The main pathways of how nutrients promote sleep-wake are through the gastrointestinal tract, precursors for serotonin and melatonin, bioactive molecules and other unidentified mechanisms. Therefore, sleep duration was used as an outcome in Chapter 3. Adapted from (133).

The first pathway through the gastrointestinal tract, various gut hormones are released after food consumption and signal to the hypothalamus in the brain via vagal nerve and consequently affect sleep. Cholecystokinin is an intestinal peptide hormone released postprandial that regulates gut motility and digestion. Cholecystokinin release was high after a HF-LC diet and induced sleepiness in 18 healthy adults after 2-3 hours (148). Ghrelin is a hormone that has numerous functions mainly stimulating appetite. Ghrelin

levels are raised before feeding and are suppressed by food ingestion. Postprandial ghrelin regulation is affected by the macronutrient content of ingested food. Evidence to date shows that carbohydrates are the most effective in suppressing ghrelin, which may be due to their rapid absorption compared to protein and fat. Whereas fat consumption show weak capacity to suppress ghrelin and protein induced prolonged ghrelin suppression (149). Ghrelin is also regulated by numerous postprandial gastric hormones such as Cholecystokinin, insulin and acetylcholine neurotransmitter. Vascular perfusion of acetylcholine to isolated stomachs of rats increased ghrelin release by ~37% and Cholecystokinin increased ghrelin release by ~200% whereas insulin decreased it by ~30% compared to controls (150). Environmental factors such as temperature and stress also influenced plasma ghrelin levels in rats (151).

In the last decade, the role of ghrelin on sleep-wake regulation has been proposed by Steiger and colleagues (152, 153) and has been highlighted for its role in sleep regulation more recently (154). Administration of ghrelin in rats increased wakefulness depending on the dose and route of administration however, in humans it depended on the time of administration and sex. Intravenous administration of ghrelin had no effect on women but promoted sleep in young and elderly men (154). When ghrelin was administered in early morning, it did not affect sleep (155) however, after one night of sleep deprivation, ghrelin plasma increased before sleep recovery (156).

Stable glucose levels during sleep are maintained through a number of mechanisms including the release of growth hormone. Ghrelin modulates sleep through its activation of hypothalamic-pituitary-adrenal axis that regulates the secretion of nocturnal growth hormone. Furthermore, peptide tyrosine is a short amino acid released postprandial that crosses the blood brain barrier and has been shown to enhance NREM sleep in animal experiments (157). The exact mechanism is unclear however it may be through its interaction with serotonin (158).

The second pathway of the effect of macronutrients on sleep regulation is through precursors for serotonin and melatonin (Figure 1.2.). Serotonin is a neurotransmitter that has many body functions and controls directly or indirectly sleep-wake cycles mainly through changes in melatonin concentration since serotonin is an intermediate product for the production of melatonin. Tryptophan is an essential amino acid that is used in the biosynthesis of proteins and is a precursor of serotonin and competes with large chain neutral amino acids (LCNAAs) to cross the blood brain barrier. The body is unable to synthesize tryptophan thus tryptophan levels depend on dietary consumption. Tryptophan is present in most protein-based foods or dietary proteins such as milk, yogurt, cheese, red meat, eggs, fish, salmon, poultry, sesame, chickpeas, almonds and

oats (159). Higher concentrations of tryptophan are favoured for its entry to the brain and thus serotonin production is upregulated promoting sleep. However, the plasma ratio of tryptophan/LCNNAs are affected by dietary carbohydrates and proteins therefore experimental studies manipulating carbohydrate intake resulting in changed sleep architecture may be mediated by the tryptophan/LCNNAs ratio (71). Furthermore, after a HC diet, insulin influences the transport of tryptophan by mediating the uptake of LCNNAs in the muscles lowering its concentration and remaining high levels of tryptophan and consequently promoting sleep.

When tryptophan is transported to the brain, the enzyme tryptophan 2,3-dioxygenase, catalyses tryptophan to formylkynurenine, which is rapidly converted to kynurenine and, finally, to niacin (vitamin B_3). Vitamin B_3 suppresses the activity of tryptophan 2,3-dioxygenase, thus leaving more tryptophan to be used in the synthesis of serotonin. 5-hydroxytryptophan is converted to serotonin by the enzyme Aromatic L-amino acid decarboxylase which needs pyridoxine (vitamin B_6) (Figure 1.2.). Serotonin is then converted to melatonin by the enzyme arylalkylamine-N-acetyltransferase which needs n-3 fatty acids (Figure 1.2.). This shows that vitamin B_3 has a role in the availability of tryptophan for the synthesis of serotonin and melatonin and vitamin B_6 and n-3 fatty acids have a role in stimulating the synthesis of serotonin and melatonin consequently regulating sleep.

The third suggested pathway is through bioactive peptides that are released after digestion and are related to the γ-aminobutyric acid (GABA) sleep promoting neurotransmitter-. However, further studies are required to confirm this pathway (133).

1.5.3.2 Foods

The use of herbs in treating insomnia (160) and promoting sleep (161) such as chamomile tea, kava-kava and valerian have been previously reviewed with a lack of supportive evidence to date (162). Few studies have assessed the effects of various foods such as milk, fatty fish, cherries and kiwifruit on sleep measures (71, 134).

Milk is considered the first to be studied relative to sleep (163). Southwell et al compared the effects of 350 ml water, 350 ml of warm milk with 5 teaspoons of Horlick powder, a malted milk drink, and no drink (control) on movements during sleep. The results showed that consumption of the warm milk reduced the number of movements compared to warm water and the control. This was consistent with another study that reported longer sleep duration and continuity after the consumption of Horlicks drink (164). This was not supported by a further study that found no difference in sleep duration after the consumption of Horlicks (165). In elderly participants, commercial milk had no effect on

sleep whereas a melatonin rich milk in a double blinded study increased morning activity, reflecting better sleep (166) and sleep efficacy was improved with reduced number of awakenings (167). The mechanisms underlying the effects of malted milk on sleep may be due to the high tryptophan and B vitamin content that are precursors of serotonin and thus the synthesis of melatonin (Figure 1.1). However, the previous studies include short intervention periods with small study groups, indicating further studies are required to confirm these effects.

Furthermore, the effects of fatty fish on sleep measures have been studied due to their high content of n-3 fatty acids that may promote tryptophan availability for serotonin synthesis (Figure 1.2.). A study investigated the effects of Atlantic salmon consumption 3 times a week for 6 months in men (168). No differences were observed in SOL between consumption of fatty fish and the control group however there was an increase in SOL from pre to post test in the control group. The consumption of oily fish was associated with better sleep quality in a cross-sectional analyses of 721 adults (169). These studies do not provide enough evidence that fatty fish consumption affects sleep and further studies are needed to explore this further.

In a randomised cross-over study, St-Onge et al investigated the effects of a controlled diet vs. ad libitum diet on sleep architecture and duration (170). Sleep duration did not differ between a controlled and ad libitum diet however, after ad libitum eating, participants had longer SOL and less SWS. Low fibre and high saturated fat and sugar intakes were associated with less SWS and more arousals. The authors suggested that a high fibre diet with low intakes of sugar and other non-fibre carbohydrates may improve sleep architecture providing insight to investigate the relationship between fruit and vegetable consumption as they are rich sources of fibre (89) and sleep. Other interventional studies exploring the effects of cherries and kiwifruit on sleep measures will be discussed in detail in section 1.6.

1.6 Sleep and fruit and vegetable consumption

Several child and adolescent studies have assessed the association between sleep measures and dietary intake including FV consumption (171-184). The association was shown to be positive in a recent meta-analysis (185). It was conducted to assess the association between sleep duration and dietary intake in children aged 2-18 years (185). Inclusion criteria included observational and experimental trials. Thirty studies were included in the systematic review and 10 in the meta-analysis with 72,054 children included. Short sleep duration was associated with lower consumption of FV and an increased consumption of FV in children was associated with sleeping adequately.

The associations between sleep measures and FV consumption are more consistent in children however, are not well characterized in adults (52). Sleep requirements differ between children, adolescents and adults (2) and there is a need for more studies to assess this relationship in adults.

Observational and experimental adult studies assessing the association between sleep measures and FV consumption are summarised in Table 1.3. and are explained in detail in Table 1.4. We used Medline, EMBASE, CINAHL, Cochrane, and PubMed databases (see Appendix A (A.1.) for search terms used) to find published studies exploring the relationships between sleep and FV consumption. Hand searches of reference lists of retrieved articles were also undertaken. A total of 49 human studies were identified with 37 cross-sectional studies, 2 prospective studies (186, 187) and only 10 interventional studies including either sleep restriction or extension (99, 188-190) or the effects of FV items on sleep measures (191-196) (Table 1.3.).

1.6.1 Sleep affects fruit and vegetable consumption: experimental studies

Sleep restriction in young healthy men increased appetite for FV by 17% for fruit and fruit juices and 21% for vegetables compared to sleep extension (99). In contrast, sleep restriction had no effect on healthy snack intake composed of 1 piece of fresh fruit and 1 packet of 40 gram dried fruit and nuts in healthy Australian men (188). Similarly, calories consumed from FV and salad did not differ between sleep restriction and baseline however, there was an interaction between race and sleep for FV intakes and salad with African Americans consuming fewer calories from FV and salad during baseline but did not differ from whites during sleep restriction (189). Tasali and colleagues studied the effects of sleep extension using a home based approach in 10 overweight adults on the desire for various foods including FV however, the study did not have a control group. Sleep extension did not change the desire for FV (190) (Table 1.4.).

1.6.2 Fruit affects sleep: experimental studies

A few studies have assessed the effects of tart cherry juice and products (191-193, 195) and kiwifruit (194) on sleep measures (Table 1.4.). However some studies had no control group to compare the effects of cherry (191, 192) and kiwifruit (194) on sleep measures whereas other studies included a control group (193, 195, 196). The previous studies included a small sample size and a short period of intervention and did not meet the scoring of methodological quality to be included in a systematic review of dietary interventions targeting sleep behaviour (134). There is a need for more well conducted interventional studies to identify the effects of FV components on sleep measures.

1.6.3 Observational studies

Table 1.4. shows that all studies assessing the associations between sleep and FV consumption were cross-sectional (37 studies) apart from 2 prospective studies (186, 187). Most of the studies were conducted in US populations and from the 37 cross-sectional studies only 3 studies were conducted in UK populations (123, 197, 198) and were published in the last ~ 3 years and only one was conducted using a nationally representative database of UK adults (123). None of the 3 studies had a primary objective of assessing the association between sleep duration and FV consumption. Testing for non-linear associations has been recommended between sleep measures and dietary intakes (52) however, no study assessed non-linear associations (Table 1.3). Therefore, there is a need for more cross-sectional studies conducted in nationally representative UK adults and assessing for non-linear associations between sleep and dietary intake.

The two prospective studies also had different objectives including assessment of the association between sleep duration and lifestyle factors (186) and sleep quality and survival in elderly (187). Additionally, Imaki et al (186) only compared the intakes of vegetables during 6 years using percentages with no analyses of prediction used to assess the association between sleep duration and vegetable consumption. Only two observational studies had their primary objective to assess the association between sleep duration and FV consumption in pregnant women (199) and Chinese older adults (≥ 65 years) (200). Another study assessed the association between sleep duration and obesity related risk factors that included FV consumption (201). No prospective study assessed the association between FV consumption as the exposure and sleep as the outcome (Table 1.3.).

Collectively, there is a dearth of studies assessing the cross-sectional and prospective associations between sleep duration and FV consumption in UK adults. Testing for non-linear associations has been recommended between sleep measures and dietary intakes (52) however, no studies have assessed non-linear associations between sleep duration and FV consumption (Table 1.3.).

Table 1.3. Summary of human studies (references) assessing the association between sleep and FV consumption in adults.

	Study type				
	Observational		Experimental (intervention)		
	Cross-sectional	Prospective	Sleep restriction	Sleep extension	Fruit intervention
Exposure/outcome not clearly stated	(202-206)				
Exposure					
Sleep	(110, 123, 197, 198, 201, 207-223)	(186, 187)	(99, 188, 189)	(99, 190)	
Diet including FV	(199, 200, 224-231)				(191-196)
Outcome					
Sleep	(199, 200, 224-231)				(191-196)
Diet including FV	(110, 123, 197, 198, 201, 207-223)	(186, 187)	(99, 188, 189)	(99, 190)	
Populations					
UK population	(123, 197, 198)				(195)
US population	(199, 201, 202, 205, 207-212, 214, 217, 225, 227, 229)		(99, 189)	(99, 190)	(193)
Other populations	(110, 200, 203, 204, 206, 213, 215, 216, 218-224, 226, 228, 230, 231)	(186, 187)	(188)		(191, 192, 194, 196)
Sleep assessment					
Subjective	(110, 123, 197-208, 210-212, 214-216, 218-231)	(186, 187)			(193)
Objective	(209, 217)		(99, 188, 189)	(99, 190)	(191, 192, 194-196)

Table 1.3. (continued) Summary of human studies (references) assessing the association between sleep and FV consumption in adults.

	Observational		Experimental (intervention)		
	Cross-sectional	**Prospective**	**Sleep restriction**	**Sleep extension**	**Fruit intervention**
Sleep measurements					
Sleep duration	(110, 123, 197-203, 205-207, 210-220, 222, 223, 225, 227-231)	(186)	(99, 188, 189)	(99, 190)	(191-196)
Sleep quality	(200, 204, 206, 208, 212, 216, 217, 221-226, 228)	(187)			(191-193, 195, 196)
Sleep timing	(209)				
Associations between sleep and FV					
Significant association	(110, 197-203, 205-210, 214, 217-220, 222, 224-226, 228, 230, 231)	(186, 187)	(99)		(191-196)
No association	(123, 204, 211-213, 215, 216, 221, 223, 227, 229)		(188, 189)	(99, 190)	
No control group				(190)	(191, 192, 194)
Primary objective of study was to assess associations between sleep and FV	(199, 200)				(191-196)
Assessed non-linear associations between sleep and FV	Not available				

Legend: FV (fruits and vegetables), UK (United Kingdom), US (United States).

Table 1.4 Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author, Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Cross-sectional studies								
Patel et al 2006 **(202)**	United States	Nurse's Health study	68,183	Subjective report of sleep duration. Sleep duration categorized to ≤5 h, 6h, 7h, 8h and ≥9h	FFQ	No adjustment	FV consumption differed between sleep duration categories in baseline characteristics	Exposure and outcome not clearly stated. The significant difference in FV consumption between sleep duration groups could be due to the numerous categories of sleep duration
Adams and Colner 2008 **(207)**	United States	College students aged 18-25 years	40,209	Subjective report of sleep duration	FV consumption (servings/d)	Not clear	Sleep duration was a significant predictor for FV intakes, increased FV intake was positively associated with sleep duration	Sleep duration was combined in a physical health model based on health issues identified by the Centers for Disease Control and Prevention
Stamatakis and Brownson 2008 **(201)**	United States	Participants aged 20-92 from rural communities in Missouri, Tennessee, and Arkansas	1203	Subjective report of sleep duration. Sleep duration categorized to <7h, 7-9h and ≥ 9h	Self-report of FV consumption (servings/d) over the past month; categorized to 1-2 servings/d, 3-4 servings/d and ≥ 5 servings/d	Age, sex, ethnicity, education, marital status, and household income	Short sleep duration was associated with low FV consumption	

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Buxton et al 2009 **(208)**	United States	Motor freight workers	542	Sleep adequacy assessed by "How often during the past 4 weeks did you get enough sleep to feel rested upon waking up"	6- items of FV (servings/d)	Clustering of workers in trucking terminals through inclusion of terminal as a random effect	Adequate sleep was associated with more servings of FV	Several confounders were not adjusted for in the model
Baron et al 2011 **(209)**	United states	Adults recruited from the community	52 adults aged 18-71 years	Sleep timing assessed using logs and wrist actigraphy for 7 d	Food log in which participants recorded all food and drinks consumed for a 7 d period	Age and sleep duration	Sleep timing was independently associated with FV consumption. Later sleep timing was associated with fewer servings of FV	Exclusion criteria did not include shift workers, this could cause report bias. Morning type diurnal preference participants were excluded providing no comparison with evening type participants
Kim et al 2011 **(210)**	United States	Women aged 35-74 years	27,983	Subjective report of sleep duration	Eating pattern was self-reported and conventional eating and snack dominance scores were calculated, HEI calculated from FFQ	Age, race, income, education, employment, marital status, children, BMI, menopause status, smoking, alcohol, physical activity, health status, stress	FV consumption (servings/d) were different among the four quartiles of conventional eating score. Short and long sleepers showed preponderance of snacks over meals related to lower intakes of FV	May have over adjusted and did not adjust for total energy intake

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Haghighatdoost et al 2012 **(110)**	Iran	Female university students aged 18-28 years	410	Subjective report of sleep duration. Sleep duration were categorized based on the tertiles of sleep duration: <6h,: 6-8h and >8h	168 –items of FFQ. Diet diversity and HEI were calculated	No adjusted variables because the study was comparing dietary intake between tertiles of sleep duration	Consumption of fruits was significantly lower in the lowest tertile (< 6 h) compared to the highest tertile (>8 h). Diversity scores of FV were significantly lower among participants in the lowest tertile.	
Hoefelmann et al 2012 **(224)**	Brazil	Workers part of a national survey	47,477	Self-report of FV (servings/week). FV were categorised to adequate or inadequate (5 or more days per week)	Subjective report of sleep quality	Socio-demographic indicators negative perception of health, wellbeing, stress, and self-reported morbidities	Inadequate FV consumption was associated with poor sleep quality	
Mosca and Aggarwal 2012 **(211)**	United States	Men older than 40 years and women older than 50 years	371	Subjective report of sleep duration and snoring (yes, no).Sleep duration categorized to (<6 h/d) and (≥ 6 h/d)	< 5 or ≥5 servings/d of FV	Age, sex, ethnicity, and marital status	No difference was shown between sleep duration categories and FV consumption. Snoring was associated with consuming less than 5 servings/day of FV	Assessment method of FV was not mentioned, may be self-report using a standardized questionnaire

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Tu et al 2012 **(203)**	China	Chinese women aged 40-70 years from the Shanghai Women's Health Study	68,832	Subjective report of sleep duration. Sleep duration categorized; ≤4h, 5h,6h, 8h, 9h and ≥10h	FFQ	Age, education level, occupational status, history of night-shift work, annual income, menopausal status, marital status, and number of live births	Fruit intake was inversely associated with short sleep duration. FV consumption was not associated with long sleep	Exposure and outcome not clearly stated
Beydoun et al 2014 **(225)**	United States	Adults aged 20-85 from the NHANES	2,459	Two 24- h dietary recalls. FV consumption (cup equivalent/d)	Subjective report of 28 items of sleep. Sleep duration was categorized; very short < 5h per night, short 5-6h per night, normal 7-8 h per night and long ≥9h per night	No adjustment	Very short, short and long sleepers consumed less FV compared to normal	
Katagiri et al 2014 **(226)**	Japan	Middle-aged female workers aged 34-65 years	3,129	151-item self-administered diet history questionnaire	PSQI	Physical activity, CES-D score, employment, smoking and BMI	High intake of vegetables were associated with good sleep quality	Analyses was not adjusted for several potential confounders e.g. age, total energy intake, SES and ethnicity
Mota et al 2014 **(204)**	Brazil	Resident physicians	72	Sleepiness assessed using the ESS. Sleep quality assessed using PSQI	Food diary for 3 non-consecutive days. FV consumption calculated using AHEI	Age and BMI	FV consumption were not correlated with ESS and PSQI	Exposure/outcome not clearly stated. Pearson correlation was used, does not provide predictions (232). Analyses was not adjusted for several potential confounders

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Chang et al 2015 **(212)**	United States	Overweight and obese pregnant women	213	Sleep was assessed by PSQI	7-items of FV assessed by the Rapid Food Screener	Not stated may be due to the use of Pearson correlation and path analyses (to investigate the mediating roles)	Sleep duration and sleep quality were not associated with FV intakes in all three trimesters. SOL was correlated to FV in the first and third trimester	
Grandner et al 2015 **(227)**	United States	Nationally representative adults	323,047	Daily servings of FV from the BRFSS	Self-report of perceived insufficient sleep, "During the past 30 d, how many days have you felt you did not get enough rest or sleep?	Not clear	Consuming <1 or 1-3 servings of FV was not associated with insufficient sleep	Adjusted variables were not clearly reported
Kurotani et al 2015 **(228)**	Japan	Workers aged 18-70 years	2025	52-item diet history questionnaire. Healthy DPs included vegetables, mushrooms, potatoes, seaweeds ,soy products and eggs	Subjective report of seep duration, difficulty initiating and maintaining sleep and sleep quality	Age, sex, site, shift work, employment, marital status, BMI, smoking, alcohol, physical activity, diabetic treatment, energy intake, skipping meals, habitual snacking at night	An inverse association was found between the healthy DPs and difficulties falling asleep at least once a week and persisted after excluding participants with severe depressive symptoms	May have over adjusted

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Mossavar-Rahmani et al 2015 **(205)**	United states	Hispanic/Latino participants aged 18-74 years	11,888	Subjective report on sleeping and waking times. Sleep duration categorized: short ≥3 h and <6 h, intermediate >6 h and ≤9h, long >9 h and ≤ 14 h	Two 24-hour dietary recalls. AHEI-2010 scores for diet quality	Age, sex, Hispanic/Latino background, income, employment status, education, depressive symptomology, and years lived in the US	Short sleepers had a lower quality diet compared to intermediate sleepers with significantly lower intakes of vegetables. Long sleepers had lower intakes of FV compared to intermediate sleepers. Participants who consumed a snack or meal 3 h before bedtime had lower intakes of vegetables compared to those who didn't	Exposure and outcome not clearly stated
Patterson et al 2016 **(197)**	United Kingdom	Adults aged 40-69 from the UK Biobank	439,933	Subjective report of sleep duration categorized; very short ≤4 h, short 5–6 h, adequate 7–8 h, and long ≥9 h	Self-report of FV consumption for the previous year	Age, sex, ethnicity, attended college and employment	Longer sleep duration was negatively associated with daily fruit intake, but positively associated with vegetable intake	FV consumption for the previous year may cause over/under reporting
Quick et al 2016 **(229)**	United States	College students aged 18-24 years	1,252	FV consumption over the past month (cups/day)	PSQI. Sleep duration categorized; <7 h/night, 7-8 h/night and ≥8 h/night	Sex, ethnicity, work time pressures, negative affect, and sleep disturbances	No difference was found in FV consumption between sleep duration groups	

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Silva et al 2016 **(213)**	Brazil	Students aged 18-39	204	Perceived sleep debt calculated (preferred weekday sleep duration – self reported weekday sleep duration)	FFQ	Age, BMI and sex	FV consumption were not associated with perceived sleep debt	
Xiao et al 2016 **(214)**	United States	Women within 5 years of childbirth aged 20-44 years	896	Subjective report of sleep duration. Sleep duration was categorized to ≤6 h,7-8h and long ≥9h	Diet was assessed by two 24-h dietary recalls. Diet quality was measured by HEI-2010	Age, ethnicity, education, marital status, poverty income ratio , weight status, years after recent childbirth, smoking , physical activity, depressive symptoms, history of breastfeeding, and diagnoses of chronic diseases	Short sleep duration was not associated with FV consumption. Long sleep duration was associated with lower consumption of total fruit and whole fruit	May have over adjusted
Doo and Kim 2017 **(215)**	Korea	Pre and post-menopausal women	17,841	Subjective report of sleep duration. Sleep duration categorized to short (≤ 6.9 h/d) and adequate (≥ 7 h/d)	One 24-hour recall	Age, education, household income, diseases, smoking, alcohol and physical activity	No differences were observed in FV consumption by sleep duration	

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
****Duke et al. 2017 (199)**	**United States**	**Pregnant**	**2942**	**FV consumption, 4 questions from the BRFSS**	**Subjective report of sleep duration**	**Age, ethnicity, education, exercise, marital status, income, employment**	**Orange & green vegetables were inversely associated with sleep duration. Total FV were not associated with sleep duration. Odds of meeting or exceeding sleep recommendation increased with each unit increase in total FV (OR=1.05 95% CI 1.003, 1.092)**	**Recall of FV intakes was for the past month which is based on memory and may cause over or underreporting**
Kleiser et al 2017 **(216)**	Bavaria, Germany	Bavarian adults aged ≥18	814	PSQI	Three 24-hour dietary recalls (2 weekdays, one weekend)	Age, sex BMI, education, smoking physical activity, TV/PC use and season	Sleep duration was not associated with FV consumption	
Mossavar-Rahmani et al 2017**(217)**	United States	Hispanic/Latino participants aged 18-74 years from 4 US cities	2140	Sleep measured by actigraphy for 7 consecutive days. Sleep duration categorized; short (<6 h), intermediate (= 6 and <8 h) and long (≥ 8 h). Sleep fragmentation index calculated	Two 24-hour dietary recalls. AHEI-2010 scores for diet quality	Age, sex, site, ethnic background, employment depression and log daily energy intake	Short sleepers had the lowest intake of whole fruit. Sleep efficiency was positively associated with whole fruit intake and sleep fragmentation index was negatively associated with whole fruit intake	

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Pérez-Rodrigo et al 2017 **(230)**	Spain	Adults aged 18-64	1,617	24-h diet recall, a 3-day food record aided by a tablet device. Four DPs identified; traditional (high in FV), Mediterranean (high in FV), snack and dairy	Subjective report of sleep duration. Three lifestyle patterns identified ; "Mixed diet-physically active-low sedentary lifestyle pattern", a "Not poor diet-low physical activity-low sedentary lifestyle pattern" and a "Poor diet-low physical activity-sedentary lifestyle pattern"	Age	Sleep duration differed between the 3 lifestyle patterns in men and women. In both men and women, mean sleep duration was the highest in the "Not poor diet-low physical activity-low sedentary lifestyle pattern"	Two DPs were identified with high intakes of FV. Analyses was not adjusted for several potential confounders
Potter et al 2017 **(123)**	United Kingdom	Adults aged 19-65 years from the NDNS	1,615	Subjective report of sleep duration	4-day food diary	Age, sex, smoking, ethnicity and SES	Sleep duration was not associated with FV consumption	Did not adjust for total energy intake
Timmermans et al 2017 **(218)**	Europe	Adults (mean age 52 years)	5,900	Subjective report of sleep duration	FFQ	Age, sex, education and self-rated health	Longer sleep duration was associated with lower fruit consumption (OR=0.89, 95% CI=0.79; 0.99)	
Van Lee et al 2017 **(206)**	Singapore	Pregnant women	497	PSQI	One 24-hour recall at 26-28 weeks of gestation. HEI-SGP to measure diet quality. DPs included FV and white rice pattern	Alcohol, physical activity, household income, education, ethnicity, energy intake, age and gravidity	Good sleep quality was associated with better diet quality and greater adherence to the FV and white rice pattern compared to poor sleep quality.	The study did not clearly state which is the exposure and outcome

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Wang et al 2017 **(231)**	China	Older adults aged 60-79 years	4,115	Inadequate fruit intake was defined as adults who ate fruit less than three times per week	Subjective report of sleep duration. Sleep duration was categorized to <7 h/d, 7-8 h/d and >8 h/d	All independent variables of socio-demographic and lifestyle variables were included in the same model thus adjusting for each other	Inadequate intake of fruits was positively associated with short and long sleep durations	The definition of inadequate fruit was not based on a reference
Gebski et al 2018 **(219)**	Polish adults	Adults aged 21-65 years	1,007 adults	Subjective report of sleep duration	Frequency of consumption of selected food groups including FV. Five DPs were derived including FV pattern and FV juices	Age, education and place of residence	In weekdays, short sleep duration was associated with lower odds of FV DP in men. In weekends, short sleep duration was associated with higher odds of FV DP in women	Analyses was not adjusted for several potential confounders
****Lee et al 2018 (200)**	**China**	**Older adults aged ≥65 years**	**5,911**	**Subjective report of the frequency of FV consumption**	**Subjective report of sleep duration and quality. Sleep duration categorised; short (<7 h), recommended (7-8 h) and long (>8 h)**	**Age, sex, marital status, education, alcohol, smoking, exercise, household income, community and province**	**Frequent FV consumption were associated with better sleep quality. Less frequent FV consumption was associated with short sleep and long sleep compared to the reference**	**Did not test for non-linear associations. Dietary recall may cause over or under reporting**
Patterson et al 2018 **(198)**	United Kingdom	Adults aged 40-69 enrolled in the UK Biobank	438,933	Subjective report of sleep duration. Sleep duration was categorized to ≤6 h/d, 7-8 h/d and ≥9 h/d	FFQ. Variables combined and a binary variable created to (<5 servings/d, ≥5 servings/d)	Age, sex, ethnicity, employment, shift work, education, urban vs. rural residence	Long sleepers with had a 62% higher odds of eating <5 servings/d of FV compared with adequate sleepers	Sleep duration and chronotype were used together as independent variables suggesting interactive effects

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Peltzer et al 2018 **(220)**	South Africa	Participants aged 40 years- 111	4,725	Subjective report of sleep duration. Sleep duration was categorized to <7 h/d, 7-8 h/d and ≥9 h/d	FV consumption were assessed with two questions, "How many servings of FV you eat on a typical day? (on any one day)" (with the help of show-cards)Inadequate FV consumption was classified as having < 5 servings/day	Not stated	Consumption of <5 servings/day of FV were associated with higher odds of short sleep duration	Authors state adjusted multinomial logistic regression but did not state the confounders
Tan et al 2018 **(221)**	Germany and Netherlands	Participants aged 20-85 years	790	Subjective report of restful sleep and sleep quality	Self-report of FV consumption. "During the last weeks, did you eat five portions of FV per day?" The answers were based on a 5-point Likert scale	Age, sex, BMI, country of origin, employment status, marital status, and education	Restful sleep was not associated with FV consumption however, in combination, restful sleep, physical activity, and FV intake were associated with increased sleep quality	
Vézina-Im et al 2018 **(222)**	Canada	Women of child bearing age 18-44 years	9,749	Subjective report of sleep duration and quality. Sleep duration was categorized to <7 h/night and ≥ 7h/ night	6-item questions to assess FV consumption	No adjustment	FV intake was associated with higher odds of having adequate sleep duration and quality sleep	

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Vézina-Im et al 2018 **(223)**	Canada	Women of child bearing age 18-44 years	9,749	Subjective report of sleep duration and quality. Sleep duration was categorized to <7 h/night and ≥ 7h/ night	6-item questions to assess FV consumption	Age, ethnicity, education, household income, marital status, employment, parity, region, season, mood disorder, FV intake, physical activity, smoking, and alcohol	FV consumption was included as an adjustment between sleep duration and quality with BMI. FV consumption was not associated in the relationship between sleep duration and quality with BMI ≥25	This study assessed the association between sleep duration and quality with BMI adjusting for several covariates including FV intakes
Prospective studies								
Imaki et al 2002 **(186)**	Japan (6 year follow-up)	Male employees aged 20-59 years	2,000	Multiple choice questionnaire: hours of sleep, 1) ≤6 h, 2) 6.1-8.9 h, 3) ≥9 h	7 –items of dietary habits including vegetable intakes in the diet 1) ample 2) none	No adjustment	The percentage of participants who slept 6h or less consumed less vegetables compared to 6.1-8.9 hours during the 6 year period of study	This study did not use any analyses for prediction such as regression analyses and only compared the intakes using percentages
Huang et al 2013 **(187)**	Taiwan (10 year follow-up)	Elderly aged ≥65 years	1865	Subjective report of sleep quality categorized; poor, fair or good	24-hour dietary recall and FFQ. Dietary diversity score derived from 6 items including FV	Age, education, BMI, physical activity and use of sleeping pills	Female poor sleepers consumed fewer vegetables compared to fair or good sleepers. Dietary diversity score and sleep quality interacted and modulated mortality with sex differences	

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Sleep restriction and extension studies								
Spiegel et al 2004 **(99)**	United States	Healthy young men	12	Men were assigned to either 4 hours of sleep for 2 consecutive nights or 10 hours of sleep for 2 consecutive nights	Participants were provided with standard hospital meals and completed a visual analogue scale for hunger and appetite for various food categories including FV	No adjustment	Appetite rating for FV increased following sleep restriction by 17% (p=0.07) for fruit and fruit juices and 21% for vegetables (p=0.02) compared to sleep extension	Short intervention period and small sample size
Sleep restriction studies								
Heath et al 2012 **(188)**	Australia	Healthy males	24	Participants lived 12 consecutive days in a sleep laboratory. 14 participants were sleep restricted to 4 h (severe), 10 participants were restricted to 6 h of sleep (moderate)	Participants were served 3 meals and 5-6 snacks daily. Snacks included 3 categories; sweet, savoury and healthy (1 piece of fresh fruit and 1 packet of 40g of dried fruit and nuts)	No adjustment	No effects of sleep restriction were found on healthy snack consumption	Short intervention period and small sample size
Spaeth et al 2014 **(189)**	United States	Healthy adults aged 21-50 years	44	In laboratory sleep restriction to 4 h (04:00-0:800) for 5 consecutive nights. Participants wore actigraph	Participants selected their meals and snacks by choosing from various menu options, selecting additional food and drink available in the laboratory suite	Age	Calories consumed from FV and salad did not differ between baselines and sleep restriction	

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
Sleep extension studies								
Tasali et al 2014 **(190)**	United States	Overweight young adults reporting sleep <6.5 h/d	10	Habitual sleep was followed for 1 week and intervention was extending sleep to 8.5 hours for 2 weeks by behavioural counselling on sleep hygiene	Desire for various foods including FV was assessed using visual analogue scales	No adjustment	Extended sleep did not change the desire for FV	No control group. Short intervention period and small sample size
Fruit intervention studies								
****Garrido et al 2009 (191)**	**Spain**	**Young, middle-aged and elderly**	**18**	**Powdered freeze-dried nutraceutical product diluted in 125 ml water equivalent to 141g Jerte Valley cherries, consumed twice a day for 3 consecutive days**	**Sleep was assessed by actigraphy. Participants wore it 3 days before the trial, during 3 days of trial and 1 day afterwards.**	**No adjustment**	**After intervention, sleep duration increased compared to baseline. Immobility increased and nocturnal activity decreased in young and elderly compared to baseline**	**No control group. Short intervention period and small sample size**
****Garrido et al 2010 (192)**	**Spain**	**Middle-aged and elderly Caucasian**	**12**	**200g of 7 different cultivars of cherries twice a day for three days**	**Wrist actigraphy wore 3 days before the trial and during 3 days of the trial**	**No adjusted variables**	**Sleep duration and immobility increased after intervention, the number of awakenings, sleep latency and nocturnal activity decreased**	**No control group. Short intervention period and small sample size**

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
**Pigeon et al 2010 (193)	United States	Healthy older adults aged ≥65 years with insomnia	15	Tart cherry juice blend or placebo consumed for 2 weeks twice a day in the morning between 8-10 am and in the evening 1-2 hours before bedtime	Sleep was assessed by an ISI and sleep diaries	No adjustment	Within groups, tart cherry juice improved ISI, SOL, sleep duration, sleep efficiency and wake after sleep onset. Between groups, tart cherry juice reduced the ISI score and wake after sleep onset with no difference in SOL, sleep duration and sleep efficiency	Short intervention period and small sample size
**Lin et al 2011 (194)	Taiwan	Participants self-reporting sleep disturbance aged 20-55 years	24	Two kiwifruits consumed 1 hour before bedtime for 4 weeks	CPSQI, sleep diary and actigraph	No adjustment	Actigraph and sleep diary, sleep duration and efficiency increased compared to baseline. Sleep diary showed a decrease in CPSQI score, waking time after sleep onset and SOL	No control group. Participants included only 2 males and 22 females. Kiwifruit consumption on sleep may differ by sex
**Howatson et al 2012 (195)	United Kingdom	Healthy adults	20	Participants consumed a tart cherry juice concentrate or placebo for 7 d	Sleep quality recorded by actigraphy and online subjective sleep diaries were collected	No adjustment	Sleep diary, cherry juice intake decreased napping time. Actigraphy, cherry juice increased time in bed , sleep duration and sleep efficiency	Short intervention period and small sample size

Table 1.4. (continued) Adult human studies assessing the relationship between sleep measures and fruit and vegetable consumption.

Author Year (Ref)	Country	Population	Sample *n*	Exposure	Outcome	Adjusted variables	Findings reported on sleep and FV	Comments
****Garrido et al 2013 (196)**	**Spain**	**Young middle-aged and elderly**	**30**	**Jerte Valley cherry based product (JVCP) consumed twice a day as lunch and dinner desserts for 5 d or a placebo**	**Sleep was assessed by actigraphy. Participants wore it 5 d before the trial, during 5 d of trial and 5 d afterwards**	**No adjustment**	**JVCP increased sleep duration and immobility in young, middle-aged and elderly compared to baseline and placebo. JVCP increased sleep efficiency in elderly compared to baseline. SOL decreased in middle-aged and elderly**	**Short intervention period and small sample size**

Legend: AHEI (Adapted Healthy Eating Index), AHEI-2010 (Alternative Healthy Eating Index), ANOVA (analyses of variance), BMI (body mass index), BRFSS (Behavioural Risk Factor surveillance System), CES-D (Centre for Epidemiological Studies Depression scale), CPSQI (Chinese version of the Pittsburgh Sleep Quality Index), CVD (cardio vascular disease), d (day), DPs (dietary patterns), ESS (Epworth Sleepiness Scale), FFQ (food frequency questionnaire), FV (fruits and vegetables), g (gram), h (hour), HEI (Healthy Eating Index), HEI-SGP (Healthy Eating Index for pregnant women in Singapore), ISI (Insomnia Severity Index), JVCP (Jerte Valley cherry based product), *n* (number), NDNS (National Diet and Nutrition Survey), NHANES (National Health and Nutrition Examination Surveys), OR (odds ratio), PSQI (Pittsburgh Sleep Quality Inventory), Ref (Reference), SES (socio-economic status), SOL (sleep onset latency).

**** BOLD row,** Key paper with main objective assessing the association between sleep measures and fruit and vegetable consumption.

1.7 Chronotype and fruit and vegetable consumption

Chronotype determinants include genetic (non-modifiable) and environmental factors (modifiable) (233). Non-modifiable determinants include rare cases of chronotype disorders such as advanced sleep-phase syndrome (234, 235). Other non-modifiable determinants include race (236) , sex (237) and age (238). Environmental factors that influence chronotype include light exposure, social interactions, urban/rural areas, and variations in the LD cycle across different latitudes and time zones (233).

Later chronotype (evening type) has been associated with less healthy behaviours such as smoking (197), physical inactivity with sedentary behaviour (198) consuming more alcohol and caffeine (from coffee and cola) compared to early chronotypes (239). Later chronotype was associated with higher risks of some diseases such as cardiovascular disease (240) type 2 diabetes (241) metabolic disorders (242) bipolar disorder (243) and obesity (198). In a recent study conducted using the UK Biobank, a large prospective population based cohort study including 433,268 adults, later chronotype was associated with higher odds of psychological disorders, diabetes, neurological disorders, gastrointestinal disorders and respiratory disorders. Additionally, later chronotype was associated with an increased risk of all-cause mortality compared to earlier chronotype (244).

These findings are of concern to public health and thus studies assessing the associations between chronotype and other lifestyle behaviours such as FV consumption are necessary. Inadequate intakes of FV were associated with later chronotype in a cross-sectional study in UK adolescents (178) and US adolescents (245). In other cross-sectional studies, later chronotype assessed by MEQ and MCTQ was associated with lower intakes of vegetables in Japanese women (246, 247). Similarly, later chronotype was associated with lower intakes of green, yellow, white vegetables and fruits in Japanese nurses (248). A representative sample of Finnish adults showed that later chronotypes assessed by a shortened version of MEQ consumed less fruit (249).

Patterson et al found that early chronotypes consumed more servings of FV compared to later chronotypes in UK adults from the UK Biobank project (197). Chronotype was self-reported by asking participants “Do you consider yourself to be 1) definitely a morning person, 2) more a morning than an evening person, 3) more an evening than a morning person, 4) definitely an evening person”. This was consistent with another recent study conducted by Patterson et al using the UK Biobank data with a difference of including sleep duration and chronotype as independent variables suggesting an

interactive effects between sleep homeostatic and circadian influence. Later chronotype and longer sleep was associated with higher odds of consuming <5 servings/days of FV compared with adequate sleep and earlier chronotype. However, earlier chronotypes and adequate sleep was associated with lower odds for all cardiovascular risk behaviours including tobacco use, physical inactivity, high sedentary behaviour and overweight/obesity except FV consumption <5 servings/day (198).

In contrast, no association was found between chronotype and vegetables and salad in German adolescents (250). Earlier chronotype assessed by MEQ was associated with lower intakes of vegetables and no association with fruit intake (251). No association was found between chronotype and FV consumption among Brazilian undergraduate students (213).

The previous studies show that later chronotypes tend to consume unhealthy diets with low intakes of FV. However, the results are contradictory and a main limitation of the previous studies is the lack of usage of objective methods to measure chronotype such as actimetry and validated dietary assessment methods. There is a necessity to assess the associations between chronotype and FV consumption using validated objective methods.

1.8 Mechanisms for the relationship between sleep and fruit and vegetable consumption

The potential mechanisms underlying the reciprocal relationship between sleep duration and FV consumption are shown in Figure 1.3. Several mechanisms have been proposed regarding the reciprocal relationship between sleep disruption and dietary intake that may subsequently lead to obesity and metabolic diseases (133, 252-257).

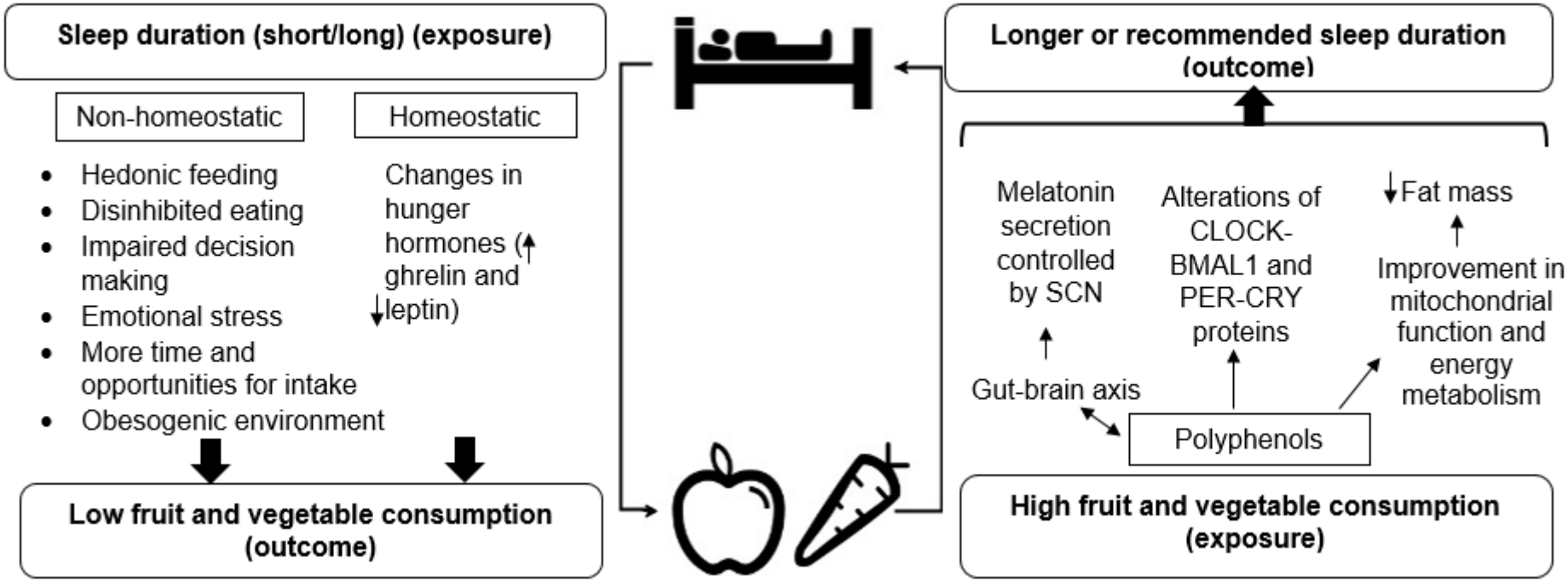

Figure 1.3. Potential mechanisms between sleep duration and fruit and vegetable consumption.

Based on previous studies, sleep disruption including short and long sleep durations may influence dietary intake through non-homeostatic and homeostatic mechanisms leading to lower consumption of FV. On the other hand, high FV consumption, through their polyphenol content through several potential pathways may be associated with longer sleep duration or sleeping the recommended hours, however, findings are contradictory. With further research, other potential mechanisms may be identified.

SCN (suprachiasmatic nuclei), CLOCK (circadian locomotor output cycles kaput), BMAL1 (brain and muscle aryl hydrocarbon receptor nuclear translocator-like 1), PER (Period), CRY (cryptochrome).

1.8.1 Homeostatic mechanisms

Sleep disruption including short and long sleep durations may influence dietary intake through both non-homeostatic and homeostatic mechanisms (Figure 1.3.). Homeostatic mechanisms include energy homeostasis mediated by satiety hormonal changes ghrelin and leptin. Leptin sends satiety signals to the appetite control centres in the brain and ghrelin sends signals from the stomach to the brain stimulating an increase in appetite (258).

A number of studies have observed associations between sleep disruption on leptin and ghrelin levels. In a laboratory study on ten healthy men, Mullington et al. observed a reduction in diurnal amplitude of leptin during the days of sleep deprivation (259). Interestingly, amplitudes of leptin returned to normal in the period of sleep recovery. Similarly, leptin levels decreased when sleep was restricted to 4 hours in 11 adults (260). Furthermore, sleep restriction reduced leptin by 18% and increased ghrelin by 28% in twelve healthy men (99). Other laboratory studies indicated an increase of ghrelin after sleep restriction (104, 261-263). However, the effects of sleep restriction on ghrelin and leptin are contradictory (156, 263-267) with a suggestion of sex differences (268). The variability in ghrelin and leptin responses to sleep restriction may be due to the small sample sizes, differences in timing of blood chemistry and analyses and variability in sleep restriction hours.

With respect to sleep duration and FV consumption mechanisms, laboratory studies showed that disrupted sleep changes appetite-related hormones ghrelin and leptin, that may increase the preference for energy-dense foods (108) leading to probably lower consumption of FV.

1.8.2 Non-homeostatic mechanisms

Non-homeostatic mechanisms have been supported with observational and experimental studies (269). In a meta-analysis, sleep deprivation was one of the most prominent lifestyle determinants of increased food intake (270). People eat more after sleep loss to compensate for the additional energetic cost of wakefulness (271). Consistently, sleep deprivation increased food purchasing in men with preference to energy-dense, rewarding foods (272). This preference for energy-dense foods may potentially lead to lower intakes of FV. Recent evidence suggests that similar to sleep restriction, long sleep duration may impair energy homeostasis through unhealthy dietary choices leading to potentially lower intakes of FV (273).

Non-homeostatic mechanisms linking sleep disruption with FV consumption include hedonic feeding, which is the consumption of food to obtain pleasure in the absence of energy deficit (274). To study the effects of sleep disruption on non-homeostatic reward-driven behaviour, brain imaging studies were conducted supporting the non-homeostatic hypothesis (275). After one night of sleep deprivation, brain activity changed in response to food stimuli and was associated with an increase in appetite (276). Furthermore, sleep restriction to 4 hours for 6 days increased the neuronal response to food stimuli and activated brain regions associated with reward (277).

Daytime sleepiness reduced the activation of ventromedial prefrontal cortex, a brain region involved in the ability to inhibit and control emotions and behaviour, when participants were shown “high calorie food” compared to “low calorie food” images (included fresh salad and FV). Additionally, this reduction in prefrontal activation predicted over-eating in women (278). Sleep restriction increased the neuronal response to “unhealthy” food images compared with “healthy” food images (that included FV) (279). This was consistent with a study that measured the effects of sleep restriction on appetite and food reward. Following sleep restriction, appetite sensations and food reward increased compared to controls (280). The previous brain imaging and experimental studies of sleep restriction provide some non-homeostatic mechanisms for sleep disruption enhancing hedonic stimulus processing in the brain and altering brain connectivity leading to food reward, food craving and affecting food decisions. The enhanced reward mechanism may promote energy-dense food consumption leading to lower intakes of FV.

It has been shown that high disinhibited eating (tendency toward overeating in response to different stimuli; for example the presence of palatable food or emotional stress (281)) mediated the relationship between disrupted sleep and weight gain (282-284). The mediating effect of disinhibition between disrupted sleep (short/long sleep durations, poor sleep quality) and weight status may be due to over-eating and less healthful food choices (285). In a cross-sectional study of 187 women and their children, disinhibition scores (higher scores indicate higher disinhibition) were negatively associated with FV in both mothers and their children (286). Consistently, in a prospective study of 2 year follow-up of men, disinhibition scores were negatively associated with fruit intake (287). These studies provide evidence that sleep disruption may lower the intakes of FV through the mediating effects of disinhibited eating.

Furthermore, emotional eating and stress were shown to influence the association between sleep duration and dietary intake (288). Disrupted sleep increases emotional reactivity (289) leading to an increase in dietary intake specifically energy-dense foods

to improve the mood and stress of individuals with their pleasing effects through the opioidergic, dopaminergic, and serotonergic systems (290) resulting in potentially lower intakes of FV. Sleep disruption deficits impulse control (291) that plays a major role in inhibiting appetitive thoughts and behaviours (256), when impulse control is altered this results in impaired decision making leading to excess dietary intake, energy-dense foods for reward potentially lower intakes of FV. Sleep disruption accompanied with an obesogenic environment – "*the sum of influences that the surroundings, opportunities, or conditions of life have on promoting obesity in individuals or populations*"(292)- may enhance behaviours including irregular eating with fewer main meals, more frequent energy-dense snacking and altered time of intake leading to potentially lower intakes of FV (52).

1.8.3 Mechanisms for effects of polyphenols on sleep

1.8.3.1 Animal studies

With the reciprocal relationship between sleep and dietary intake in mind, polyphenols in FV could influence sleep measures through several potential pathways. Polyphenols are phytochemicals that are abundant in our diets and have a probable preventive role from cardiovascular disease (293), ischemic heart disease (294), stroke (295) and cancer (296). Polyphenol profiles are complex in foods and mostly contain multiple classes of polyphenols in a single plant. The main sources of polyphenols are FV, tea, coffee, red wine, cereals, grains and soy beans however, bioavailability differ extremely between the various polyphenols. Polyphenols are classified and sub-classified based on the number of phenol rings that they contain and of the structural elements that bind these rings to one another. The main classes of polyphenols are flavonoids, phenolic acids, stilbenes, lignans and other polyphenols (297).

The direct and indirect effects of flavonoids in the brain including cerebrovascular blood flow and synaptic plasticity that improve learning and memory have been previously reviewed (298) and the role of sleep on memory has been highlighted (299) however, there are a lack of studies linking sleep with polyphenols. Some animal studies (Table 1.5.) have investigated the effects of different types of polyphenols on clock genes, circadian rhythms and sleep/wake cycle with few studies conducted in humans (see section 1.8.3.2).

Table 1.5. Summary of animal and in vitro studies (references) assessing the effects of polyphenols on sleep and their potential mechanisms.

	Potential mechanism assessed				Sleep assessed	
	Serotonin 1A receptor	**GABA receptors**	**Circadian rhythms**	**Clock gene expression**	**Sleep/wake cycles**	**Sleep duration**
In vivo	(300)	(301-305)	(306-308)	(309-313)	(300, 302-305, 314-317)	(300, 301, 303-305, 314-316, 318)
In vitro			(319)	(320)		
Polyphenol						
Flavonoids	(300)	(303)	(319)		(300, 303)	(300, 303, 318)
Resveratrol			(307, 308)	(310, 311)	(317)	
Phenolic acids						(318)
GSPEs				(309, 312, 313)		
Phlorotannins *		(301, 302)			(302)	(301)
Triphlorethol A*					(314)	(314)
Red cabbage extracts					(315)	(315)
Kiwifruit extracts		(304)			(304)	(304)
Romaine lettuce					(316)	(316)
Tea polyphenols		(305)		(320)	(305)	(305)
Cherry			(306)			

Legend: GSPEs (Grape seed proanthocyanidins extracts), GABA (γ-aminobutyric acid). * Sea weed polyphenols

The first potential mechanism of how polyphenols from FV consumption may affect sleep measures is through the gut-brain axis (Figure 1.3.) via serotonin and GABA receptors, consequently affecting nocturnal secretion of melatonin from the pineal gland controlled by the SCN (Figure 1.3.). Wang et al investigated the effects of spinosin, a C-glycoside flavonoid of Semen Ziziphi spinosae, a herb that has been used to treat insomnia and other diseases, on sleep via serotonin 1A receptor (5-hydroxytryptamine, 5-HT_{1A}) in Male Sprague–Dawley rats (300). Spinosin reduced SOL and increased NREM sleep and sleep duration and increased REM sleep time.

Other studies found that different polyphenols modulated sleep via GABA receptors. Polyphenols such as phlorotannins (301, 302) and Triphlorethol A (seaweed polyphenols) (314), red cabbage extracts (315) and kiwifruit extracts (304) decreased SOL and increased sleep duration via GABA receptors in mice. Other polyphenols such as bioflavonoids extracts from *Rhus parviflora* referred as Tintidikah, a medicinal plant used in south Asia were the most potent components in decreasing SOL and increasing sleep duration via GABA receptors (303). Seeds of *Ziziphus mauritiana*, a hypnotic widely used in Asian countries, contained flavonoids and phenolic acids that increased sleep duration in mice administered with sodium pentobarbital (318). Furthermore, the seed and leaf extracts derived from romaine lettuce potentiated the pentobarbital-induced sleeping behaviour in mice (316). In contrast, GABA in black tea did not decrease SOL induced by sodium barbital, a hypnotic, in mice but SOL was decreased and sleep duration was increased with sodium pentobarbital, a hypnotic (305). Collectively, the previous animal studies found that different polyphenols via serotonin and GABA receptors decreased SOL and increased sleep duration however, further human studies are required to confirm this.

Since the circadian system and their clock genes are intertwined with the sleep/wake cycle (1), the second potential mechanism of how polyphenols derived from FV consumption may influence sleep duration is through effects on circadian rhythms, clock gene expression and peripheral clocks (Figure 1.3.). An animal study investigated the effects of resveratrol, a dietary polyphenol present in a variety of foods including FV, on circadian period and body temperature (307). Compared to controls, resveratrol supplementation for 2 weeks in constant dark condition in primate grey mouse lemur shortened free-running period, reduced mean body temperature and locomotor activity indicating that resveratrol supplementation influences the circadian clock of those animals. Limitations of the study including the short intervention period and small number of mice (n=13) requires further exploration. However, Pifferi et al extended the

resveratrol supplementation for 4 weeks in another study (308) and observed a reduction of locomotor activity onset in dark conditions suggesting a better synchronisation.

The effects of resveratrol supplementation on clock genes was investigated in several animal studies. The expression of clock genes PER1, PER2 and BMAL1 were increased in cultured Rat-1 cells with resveratrol treatment for 8 hours (310). Resveratrol reversed the change induced by HF feeding in the expression of REV-ERBα in adipose tissue indicating that resveratrol polyphenol targets the clock genes and thus influences sleep. (311).

Pifferi et al observed an increased proportion of active-wake time during the resting phase (light) of the sleep/wake cycle after 3 weeks of resveratrol supplementation in mice. Negligible changes in active-wake time during the active phase (dark) of the sleep/wake cycle suggested that resveratrol activity depends largely on the time of administration (317). This was consistent with another study that noted that resveratrol administration on male rats behaved as an antioxidant during the night and as a pro-oxidant during day-time (321).

Furthermore, grape seed proanthocyanidins extracts (GSPEs) treatment maintained nocturnal melatonin levels and modulated circadian rhythms when it was administered at the start of the day, rather than at night (309). GDPEs administration for 21 days in healthy rats and in rats with diet-induced obesity, clock genes were overexpressed positively with a dose-dependent manner. In addition, BMAL1 protein increased and PER2 was overexpressed whereas REV-ERBα was repressed in the liver, gut and white adipose tissue in healthy rats. This was also observed in the liver and gut of diet-induced obesity rats (312). GDPEs administration modulated clock genes in rat liver by increasing BMAL1 only when administered when the light was turned off suggesting also time-dependency effects (313). The effectiveness of polyphenols during periods of the day could be due to the discrepant functionality of the SCN. It has been shown that SCN cells are extensively coupled during the day, when the cells exhibit synchronous neural activity, but minimally coupled during the night, when the cells are electrically silent (322).

Tea polyphenols were capable of manipulating circadian clock genes by enhancing BMAL1 and ameliorated neural redox imbalance and mitochondrial dysfunction (320). The intake of cherry nutraceutical product decreased diurnal activity and increased nocturnal activity in young and old rats (representative of nocturnal animals). In contrast, the opposite effects were observed for ringdoves (representative of diurnal animals) indicating that effects are modulated depending on the nature of the animals' circadian rhythms (306). The previous animal studies showed that polyphenol administration

modulated the circadian system through circadian rhythms, molecular clocks and the sleep/wake cycle with dose and time dependency and possible sex differences providing insight that polyphenols may influence sleep duration.

Since the metabolic state of a cell is coupled to the molecular clock, diet may modify rhythmic cellular activities (88). In light of this, the third potential mechanism (Figure 1.3.) of how polyphenols from FV may affect sleep is by activation of pathways that promote silent mating type information regulation 2 homolog 1 (SIRT1) protein expression (323). SIRT1 modulates the ventromedial hypothalamic clock, a brain region that contains neuronal food-synchronized clocks that contribute to regulation of the circadian rhythm in feeding behaviour (324). SIRT1 has a central role for reactive oxygen species mainly produced as a consequence of mitochondrial functions (325). It has been identified that several polyphenols, such as resveratrol, act as dietary activators of SIRT1 (323). In turn, SIRT1 binds CLOCK-BMAL1 and promote the degradation of PER2 (326) thus influencing sleep duration. Alternatively, it has been suggested that resveratrol through its action on SIRT1 improves mitochondrial function and energy metabolism by decreasing fat mass that may lead to changes in sleep duration (317).

The previous animal studies showed that polyphenols modulated sleep through several potential mechanisms however, there is a need for human studies to confirm these mechanisms.

1.8.3.2 Human experimental and observational studies

The effects of FV consumption on sleep may be due to their high content of melatonin and serotonin (327). Tart cherry juice has been shown to increase urinary melatonin concentrations in humans (193) however, this is yet to be confirmed. Alternatively, the effects of polyphenols on sleep measures may be through their antioxidant content reducing oxidative stress and improving sleep quality (71). St-Onge suggested that plant based diets improve mitochondrial function, energy metabolism, body composition, lower body fat and abdominal adiposity, consequently this may potentially improve sleep quality (328). However, this was not specifically for FV consumption but diets high in plants.

The effects of different polyphenols on sleep architecture and sleep measures have been conducted in few human experimental studies (Table 1.6.). Human experimental studies provide conflicting results with some showing an improvement in sleep measures after polyphenol administration and others not showing any effects. These mixed results may be due to the diverse intervention periods, different types of polyphenols and doses. The longest intervention period was 90 days (329) and longer intervention studies are

required. Furthermore, polyphenol effects from supplements differ from their effects from foods relatively due to their bioavailability and concentration (330). Another probable reason for the distinctive results is the small number of participants, different study designs and participants. More effects were shown in participants reporting sleep disturbances, pre-hypertensive and memory impairment than healthy adults. Experimental trials on participants with sleep problems differ from healthy free-living individuals; therefore, it is required to consider the potential for non-representative samples taking part in experimental studies.

Table 1.6. Adult human interventional studies exploring the effects of polyphenols on sleep.

Author, Year (REF)	Study type	Population	Sample *n*	Polyphenol intervention	Intervention period	Findings reported on polyphenol effect on sleep
Kuratsune et al 2010 (331)	Double-blind, placebo-controlled, cross-over	Healthy men with mild sleep complaint	21	Crocetin, active carotenoid	Two intervention periods of 2 weeks each separated by a 2-week washout	Actigraphic data showed a reduction in the number of wakening episodes compared to placebo. Subjective data showed improvement in sleep quality
Wightman et al 2015 (332)	Randomised, double-blind, placebo-controlled, parallel	Adults aged 18-30 years	60	Resveratrol	28 days	No effect on PSQI score or its seven factors
Park et al 2017 (333)	Double-blind, placebo-controlled, cross-over	Healthy adults	9	Chlorogenic acids, most abundant polyphenol in coffee	5 days	Shortened SOL compared with the control with no effect on sleep architecture
Herrlinger et al 2018 (329)	Double-blind, placebo-controlled, parallel	Older adults with age associated memory impairment	90	Spearmint extract containing 24% total polyphenols	90 days	Improved the ability to fall asleep, alertness and behaviour following wakefulness compared to controls
Um et al 2018 (334)	Randomised, double-blind, placebo-controlled, parallel	Adults with subjective sleep disturbances	24	Phlorotannin	One week	Sleep duration increased compared to placebo however no effects were shown on the total PSQI score
Romain et al 2017 (335)	Randomised, double-blind, placebo-controlled, parallel	Overweight and obese adults	33	Holisfiit®, a polyphenol-rich extract-based food supplement developed from FV	16 weeks	Awakening during the night improved by 38%, total sleep duration by 50%, and sleep quality by 43% compared to baseline and subjective sleep complaints improved significantly compared to controls

Table 1.6. (continued) Adult human interventional studies examining the effects of polyphenols on sleep.

Author, Year (REF)	Study type	Population	Sample *n*	Polyphenol intervention	Intervention period	Findings reported on polyphenol effect on sleep
Uddin et al 2018 (336)	Randomised, double-blind, placebo-controlled, cross-over	Pre-hypertensive adults	12	Fruitflow® supplements, tomato extract	24-hour period	Both systolic and diastolic blood pressure were lower after FruitFlow® consumption compared to placebo in the wake period whereas during the sleep period, the effect was only shown for systolic blood pressure only
Grassi et al 2016 (337)	Randomised, double-blind, cross-over	Healthy adults	32	Flavanol-rich chocolate	Consumption of (high or poor flavanol chocolate bars) after one night of total sleep deprivation	High-flavanol chocolate bar reduced high systolic and diastolic blood pressure caused by sleep deprivation compared to low-flavanol chocolate bar consumption
Bigelman et al 2011 (338)	Randomised, double-blind, placebo-controlled, cross-over	Healthy adults conducting military physical training	58	Quercetin	6 weeks	No effects on sleep quality

Legend: *n* (number), PSQI (Pittsburgh Sleep Quality Index), REF (reference), SOL (sleep onset latency).

Few observational studies have assessed the associations between isoflavones, a polyphenol mainly found in soybeans and legumes, with sleep measures (339, 340). Cui et al assessed the cross-sectional association between isoflavone intake and self-reported sleep duration and quality in 1076 Japanese adults (339). High intakes of isoflavones were associated with adequate sleep duration (7-8 hours) and better sleep quality. In contrast, a longitudinal study showed that the highest quartile of soy isoflavone intake was associated with lower odds of long sleep duration (≥ 9 hours/night) and lower odds of falling asleep during daytime in women only. There was a persistent inverse association between isoflavone intake and sleep duration suggesting these effects are due to the estrogenic contents of isoflavones (340).

To our knowledge, no other observational studies have explored the associations between dietary polyphenols and sleep measures despite the abundancy of animal studies showing the effects of polyphenols on sleep. The limited number of longitudinal epidemiological studies in this area suggests the need for cohort studies with validated dietary intake measures to clarify the associations between dietary polyphenols and sleep measures.

Overall this literature review has shown that sleep disruption has detrimental influences on health and dietary intake. Sleep duration and FV consumption are potentially linked however, numerous knowledge gaps (Table 1.7.) were identified and few studies have been conducted in UK adults.

Table 1.7. Identified gaps in the literature and how they were addressed in this thesis.

Section	Identified gaps	Gap addressed in this thesis	Chapter	Hypothesis based on previous results from the literature
Section 1.7	No study assessed the associations between objective measures of sleep and chronotype and FV consumption using a validated dietary assessment tool in healthy UK adults	Cross-sectional associations using objective measures of sleep and chronotype were assessed with FV consumption using a validated dietary assessment method in healthy UK adults	2	Sleep duration positively associated with FV consumption. Later chronotype associated with lower consumption of FV
Section 1.8.3	No prospective study has assessed the associations between FV items and their polyphenol content with sleep duration in UK adults	Prospective associations between FV intakes and their polyphenol content with subsequent sleep duration was explored using the UK Women's Cohort Study (UKWCS).	3	FV consumption and their polyphenol consumption positively associated with sleep duration
Section 1.6 .3	No cross-sectional study assessed the non-linear associations between sleep duration and FV consumption in a nationally representative sample of UK adults	Cross-sectional and non-linear associations assessed between sleep duration and FV consumption in a nationally representative sample of UK adults	4	Short and long sleepers consume less FV compared to the reference group
Section 1.6.3	No prospective study has assessed the associations between sleep duration and FV consumption, as well as potential non-linear associations	Explored both cross-sectional and prospective associations between sleep duration and FV intakes in UK women	5	Short and long sleepers consume less FV compared to the reference group

1.9 Thesis aim

This project aims to assess the cross-sectional and prospective associations between sleep duration and FV consumption in UK adults.

1.9.1 Thesis objectives

A limitation of many chronotype and dietary intake studies is the lack of objective methods (see section 1.7). Furthermore, the associations between sleep measures, chronotype and FV consumption has not been assessed using objective measures in UK adults.

1. To assess the cross-sectional associations between objective sleep measures, chronotype and FV consumption in UK adults.

No prospective study has assessed the associations between FV items and their polyphenol content with sleep duration in UK adults (see Table 1.3.). This knowledge gap was addressed by the second objective.

2. To investigate the prospective associations between FV intakes and their polyphenol content with subsequent sleep duration using the UK Women's Cohort Study (UKWCS).

Most cross-sectional studies assessing associations between sleep duration and dietary intake were conducted in US populations with no study in UK adults assessing potential non-linear associations (see Table 1.3.). This gap was addressed by using a nationally representative data set of UK adults.

3. To examine the cross-sectional non-linear association between sleep duration and FV intakes and their associated biomarkers in UK adults using the National Diet and Nutrition Survey (NDNS).

Causal relationships cannot be inferred from cross-sectional studies and prospective studies help to clarify associations. Among UK adults, no prospective study has assessed the associations between sleep duration and FV consumption, as well as potential non-linear associations (see Table 1.3.). Therefore, I used the UKWCS to address this gap.

4. To explore both cross-sectional and prospective non-linear associations between sleep duration and FV intakes in UK women.

Thesis framework addressing the previous objectives are shown in Figure 1.4.

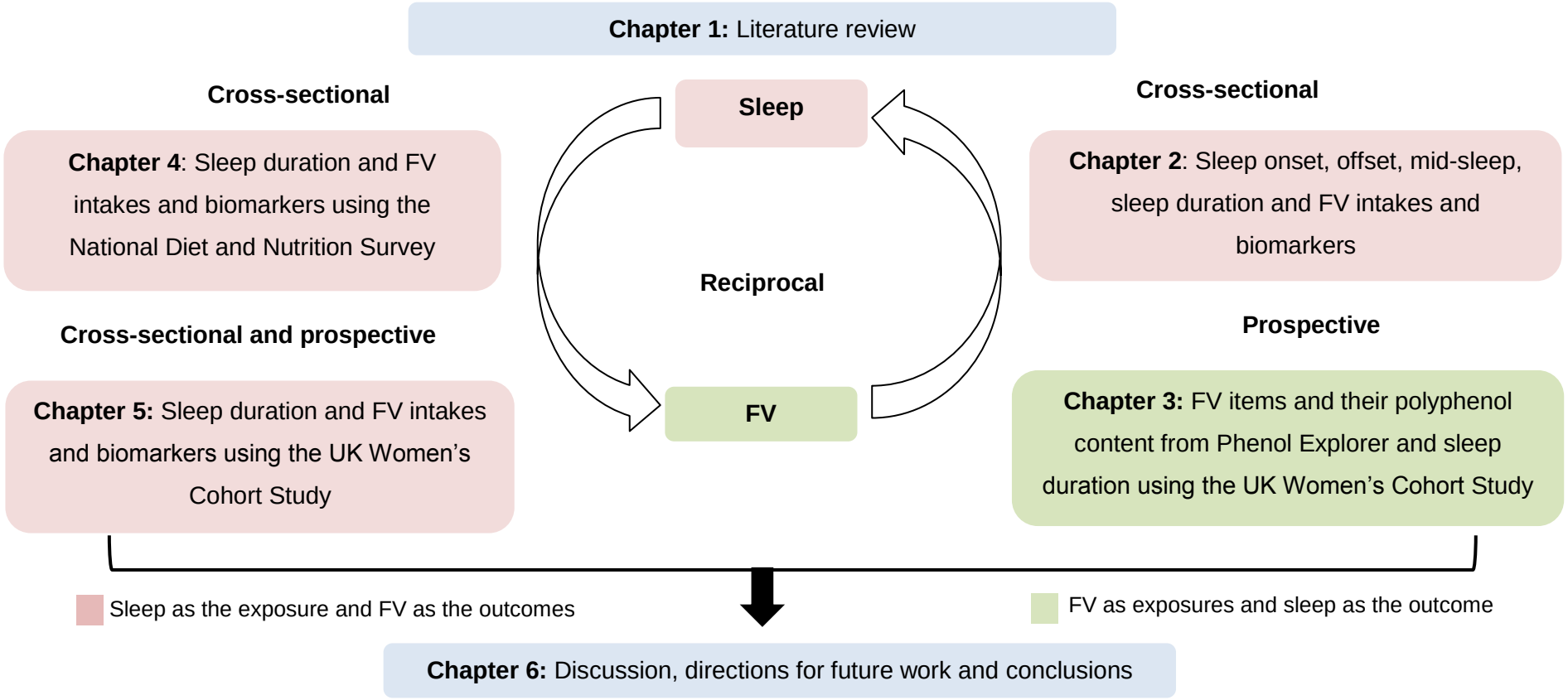

Figure 1.4. Thesis framework.

FV (fruits and vegetables)

1.10 Rationale of the databases used in this thesis

1.10.1 Chapter 2 database

As shown in Table 1.7., a knowledge gap was found in section 1.7. The gap is that no study assessed the associations between objective measures of sleep and chronotype and FV consumption using a validated dietary assessment tool in healthy UK adults. Therefore, in Chapter 2, sleep measures were assessed using objective measures and FV consumption was assessed using a validated dietary assessment tool in healthy UK adults.

1.10.2 The UK Women's Cohort Study (UKWCS) (chapters 3 and 5)

The UKWCS is a large cohort that was developed to explore links between diet and chronic diseases and has two main contact phases that are explained in detail in chapters 3 and 5. From the literature review, two main gaps were identified (see Table 1.7.) including the absence of prospective studies assessing the associations between FV items and their polyphenol content with sleep duration using large cohorts of UK adults and between sleep duration as the exposure and FV consumption as the outcomes.

We used the UKWCS for 4 reasons. First, the UKWCS includes a large sample of UK women that overcomes the limitation of small sample sizes and ensures that the analyses are not underpowered. Second, information regarding vegan/vegetarian status were collected in both contact phases which aided in conducting sensitivity analyses in both chapters 3 and 5. Third, the UKWCS is a large prospective cohort which includes health-conscious women with wide diversity in dietary intakes, which facilitates clarifying the associations between FV intakes and sleep duration. Fourth, dietary assessment in phase 1 of the UKWCS was conducted using food frequency questionnaires (FFQ) with several FV items. These FV items helped in calculating the polyphenol content separately and identify the associations with sleep duration (Chapter 3).

1.10.3 The National Diet and Nutrition Survey (NDNS) (Chapter 4)

The NDNS is a government-commissioned rolling programme that started in 1992 to assess diet, nutrient intake and nutritional status of the UK population. In the literature review, we found that no study assessed the non-linear associations between sleep duration and FV consumption using a nationally representative sample (see Table 1.7.). Therefore, the NDNS was used in this thesis for 3 reasons. First, the adults in the NDNS represent the UK population. Second, the NDNS disaggregated foods containing FV into

their components which helped in assessing total FV intake. Third, the methods used to assess sleep and FV consumption were consistent to the second phase of the UKWCS (Chapter 5) providing consistency between Chapter 4 and Chapter 5.

References of Chapter 1

1. Potter GD, Skene DJ, Arendt J, et al. Circadian Rhythm and Sleep Disruption: Causes, Metabolic Consequences, and Countermeasures. *Endocrine Reviews*, 2016, **37**(6), pp.584-608.

2. Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*, 2015, **1**(1), pp.40-43.

3. Centers for Disease Control and Prevention. *Sleep and Sleep disorders* [online]. 2018. [Accessed 25 January 2019]. Available from: https://www.cdc.gov/sleep/index.html

4. Bin YS, Marshall NS and Glozier N. Secular trends in adult sleep duration: a systematic review. *Sleep Medicine Reviews*, 2012, **16**(3), pp.223-30.

5. Bin YS, Marshall NS and Glozier N. Sleeping at the Limits: The Changing Prevalence of Short and Long Sleep Durations in 10 Countries. *American Journal of Epidemiology*, 2013, **177**(8), pp.826-833.

6. Youngstedt SD, Goff EE, Reynolds AM, et al. Has adult sleep duration declined over the last 50+ years? *Sleep Medicine Reviews*, 2016, **28**, pp.69-85.

7. Hoyos CM, Glozier N and Marshall NS. Recent Evidence on Worldwide Trends on Sleep Duration. *Sleep Epidemiology*, 2015, **1**(4), pp.195-204.

8. Matricciani L, Bin YS, Lallukka T, et al. Past, present, and future: trends in sleep duration and implications for public health. *Sleep Health*, 2017, **3**(5), pp.317-323.

9. The Sleep Council. *The Great British bedtime report* [online]. 2013. [Accessed 17 May 2017]. Available from: https://www.sleepcouncil.org.uk/wp-content/uploads/2013/02/The-Great-British-Bedtime-Report.pdf.

10. The Sleep Council. *The Great British bedtime report* [online]. 2017. [Accessed 13 June 2017]. Available from: https://sleepcouncil.org.uk/wp-content/uploads/2018/04/The-Great-British-Bedtime-Report-2017.pdf

11. Basner M, Spaeth AM and Dinges DF. Sociodemographic characteristics and waking activities and their role in the timing and duration of sleep. *Sleep*, 2014, **37**(12), pp.1889-906.

12. Simonelli G, Marshall NS, Grillakis A, et al. Sleep health epidemiology in low and middle-income countries: a systematic review and meta-analysis of the prevalence of poor sleep quality and sleep duration. *Sleep Health*, 2018, **4**(3), pp.239-250.

13. Hafner M, Stepanek M, Taylor J, et al. Why Sleep Matters-The Economic Costs of Insufficient Sleep: A Cross-Country Comparative Analysis. *Rand Health Q*, 2017, **6**(4), p.11.

14. WHO. *Diet, nutrition and the prevention of chronic diseases* [online]. 2003. [Accessed 5 September 2016]. Available from: http://apps.who.int/iris/bitstream/handle/10665/42665/WHO_TRS_916.pdf?sequence=1

15. United States Department of Agriculture. *ChooseMyPlate* [online]. 2019. [Accessed 5 February 2019] . Available from: https://www.choosemyplate.gov

16. Australian Institute of Health and Welfare. *Australia's food & nutrition* [online]. 2012. [Accessed 8 February 2019]. Available from:

https://www.aihw.gov.au/getmedia/0c26b145-81fa-4a94-af38-d52515885a07/12504.pdf.aspx?inline=true ..

17. Health Canada. *Eating Well with Canada's Food Guide* [online]. 2011. [Accessed 8 February 2019]. Available from: https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/fn-an/alt_formats/hpfb-dgpsa/pdf/food-guide-aliment/print_eatwell_bienmang-eng.pdf

18. Food and Agriculture Organization of the United Nations. *The official dietary guidelines (Danish: De officielle kostråd)* [online]. 2013. [Accessed 7 February 2019]. Available from: http://www.fao.org/nutrition/education/food-dietary-guidelines/regions/countries/denmark/en/

19. Public Health England in association with the Welsh Government, Food Standards Scotland and the Food Standards Agency in Northern Ireland. *Eatwell Guide* [online]. 2016. [Accessed 9 February 2019]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/528193/Eatwell_guide_colour.pdf.

20. WHO Regional Office for Europe. *Comparative analysis of nutrition policies in WHO European Member States.* [online]. 2003. [Accessed 6 January 2019]. Available from: https://www.who.int/nutrition/publications/policies/comparative_analysis_european/en/.

21. Hall JN, Moore S, Harper SB, et al. Global Variability in Fruit and Vegetable Consumption. *American Journal of Preventive Medicine*, 2009, **36**(5), pp.402-409.

22. Bates B, Lennox A, Prentice A, et al. *National Diet and Nutrition Survey Results from years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009-2011/2012).* [online]. 2014. [Accessed 15 September 2016]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/594361/NDNS_Y1_to_4_UK_report_full_text_revised_February_2017.pdf.

23. Bates B, Cox L, Nicholson S, Page P, Prentice A, Steer T and Swan G. *National Diet and Nutrition Survey Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013 –2013/2014)* [online]. 2016. [Accessed 9 October 2017]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/551352/NDNS_Y5_6_UK_Main_Text.pdf.

24. Bates B, Collins D, Cox L, Nicholson S, Page P, Roberts C, Steer T, and Swan G. *National Diet and Nutrition Survey Years 1 to 9 of the Rolling Programme (2008/2009 – 2016/2017): Time trend and income analyses* [online]. 2019. [Accessed 7 March 2019]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/772434/NDNS_UK_Y1-9_report.pdf.

25. Candari CJ, Cylus J, Nolte E. *Assessing the economic costs of unhealthy diets and low physical activity.An evidence review and proposed framework* [online]. 2017. [Accessed 2 January 2019]. Available from: http://www.euro.who.int/__data/assets/pdf_file/0004/342166/Unhealthy-Diets-ePDF-v1.pdf?ua=1

26. Popkin BM, Kim S, Rusev ER, et al. Measuring the full economic costs of diet, physical activity and obesity-related chronic diseases. *Obesity Reviews*, 2006, **7**(3), pp.271-293.

27. Cadilhac DA, Magnus A, Sheppard L, et al. The societal benefits of reducing six behavioural risk factors: an economic modelling study from Australia. *BMC Public Health*, 2011, **11**, p.483.

28. Ekwaru JP, Ohinmaa A, Loehr S, et al. The economic burden of inadequate consumption of vegetables and fruit in Canada. *Public Health Nutrition*, 2017, **20**(3), pp.515-523.

29. Scarborough P, Bhatnagar P, Wickramasinghe KK, et al. The economic burden of ill health due to diet, physical inactivity, smoking, alcohol and obesity in the UK: an update to 2006-07 NHS costs. *Journal of Public Health (Oxford,England)*, 2011, **33**(4), pp.527-535.

30. Cappuccio FP, Taggart FM, Kandala NB, et al. Meta-analysis of short sleep duration and obesity in children and adults. *Sleep*, 2008, **31**(5), pp.619-26.

31. Chen X, Beydoun MA and Wang Y. Is sleep duration associated with childhood obesity? A systematic review and meta-analysis. *Obesity (Silver Spring)*, 2008, **16**(2), pp.265-74.

32. Fatima Y, Doi SA and Mamun AA. Longitudinal impact of sleep on overweight and obesity in children and adolescents: a systematic review and bias-adjusted meta-analysis. *Obesity Reviews*, 2015, **16**(2), pp.137-49.

33. Ruan H, Xun P, Cai W, et al. Habitual Sleep Duration and Risk of Childhood Obesity: Systematic Review and Dose-response Meta-analysis of Prospective Cohort Studies. *Scientific Reports*, 2015, **5**, p.16160.

34. Wu Y, Gong Q, Zou Z, et al. Short sleep duration and obesity among children: A systematic review and meta-analysis of prospective studies. *Obesity Research Clinical Practice*, 2017, **11**(2), pp.140-150.

35. Fatima Y, Doi SA and Mamun AA. Sleep quality and obesity in young subjects: a meta-analysis. *Obesity Reviews*, 2016, **17**(11), pp.1154-1166.

36. Mander BA, Winer JR and Walker MP. Sleep and Human Aging. *Neuron*, 2017, **94**(1), pp.19-36.

37. Wu Y, Zhai L and Zhang D. Sleep duration and obesity among adults: a meta-analysis of prospective studies. *Sleep Medicine*, 2014, **15**(12), pp.1456-62.

38. Itani O, Jike M, Watanabe N, et al. Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression. *Sleep Medicine*, 2017, **32**, pp.246-256.

39. Jike M, Itani O, Watanabe N, et al. Long sleep duration and health outcomes: A systematic review, meta-analysis and meta-regression. *Sleep Medicine Reviews*, 2018, **39**, pp.25-36.

40. Liu W, Zhang R, Tan A, et al. Long sleep duration predicts a higher risk of obesity in adults: a meta-analysis of prospective cohort studies. *Journal of Public Health (Oxford,England)*, 2018, **fdy135**, pp.1-11.

41. Zhao H, Yin JY, Yang WS, et al. Sleep duration and cancer risk: a systematic review and meta-analysis of prospective studies. *Asian Pacific Journal of Cancer Prevention*, 2013, **14**(12), pp.7509-15.

42. Erren TC, Morfeld P, Foster RG, et al. Sleep and cancer: Synthesis of experimental data and meta-analyses of cancer incidence among some 1,500,000 study individuals in 13 countries. *Chronobiology International*, 2016, **33**(4), pp.325-50.

43. Ma QQ, Yao Q, Lin L, et al. Sleep duration and total cancer mortality: a meta-analysis of prospective studies. *Sleep Medicine*, 2016, **27-28**, pp.39-44.

44. Cappuccio FP, D'elia L, Strazzullo P, et al. Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. *Diabetes Care*, 2010, **33**(2), pp.414-20.

45. Li W, Wang D, Cao S, et al. Sleep duration and risk of stroke events and stroke mortality: A systematic review and meta-analysis of prospective cohort studies. *International Journal of Cardiology*, 2016, **223**, pp.870-876.

46. Cappuccio FP, Cooper D, D'elia L, et al. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *European Heart Journal*, 2011, **32**(12), pp.1484-92.

47. Kwok CS, Kontopantelis E, Kuligowski G, et al. Self-Reported Sleep Duration and Quality and Cardiovascular Disease and Mortality: A Dose-Response Meta-Analysis. *Journal of the American Heart Association*, 2018, **7**(15), p.e008552.

48. Cappuccio FP, D'elia L, Strazzullo P, et al. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. *Sleep*, 2010, **33**(5), pp.585-92.

49. Da Silva AA, De Mello RG, Schaan CW, et al. Sleep duration and mortality in the elderly: a systematic review with meta-analysis. *BMJ Open*, 2016, **6**(2), p.e008119.

50. Gallicchio L and Kalesan B. Sleep duration and mortality: a systematic review and meta-analysis. *Journal of Sleep Research*, 2009, **18**(2), pp.148-58.

51. Liu TZ, Xu C, Rota M, et al. Sleep duration and risk of all-cause mortality: A flexible, non-linear, meta-regression of 40 prospective cohort studies. *Sleep Medicine Reviews*, 2017, **32**, pp.28-36.

52. Dashti HS, Scheer FA, Jacques PF, et al. Short sleep duration and dietary intake: epidemiologic evidence, mechanisms, and health implications. *Advances in Nutrition*, 2015, **6**(6), pp.648-59.

53. Muraki I, Imamura F, Manson JE, et al. Fruit consumption and risk of type 2 diabetes: results from three prospective longitudinal cohort studies. *BMJ*, 2013, **347**, p.f5001.

54. He F, Nowson C, Lucas M, et al. Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies. *Journal of Human Hypertension*, 2007, **21**(9), pp.717-728.

55. Hu D, Huang J, Wang Y, et al. Fruits and vegetables consumption and risk of stroke: a meta-analysis of prospective cohort studies. *Stroke*, 2014, **45**(6), pp.1613-9.

56. World Cancer Research Fund / American Institute for Cancer Research. *Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective.* [online]. 2007. [Accessed 6 January 2016]. Available from: http://discovery.ucl.ac.uk/4841/1/4841.pdf

57. Lock K, Pomerleau J, Causer L, et al. The global burden of disease attributable to low consumption of fruit and vegetables: implications for the global strategy on diet. *Bulletin of the World Health Organization*, 2005, **83**(2), pp.100-8.

58. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and

dose-response meta-analysis of prospective studies. *International Journal of Epidemiology*, 2017, **46**(3), pp.1029-1056.

59. WHO. *Increasing fruit and vegetable consumption to reduce the risk of non-communicable diseases* [online]. 2017. [Accessed 8 February 2019]. Available from: https://www.who.int/elena/titles/fruit_vegetables_ncds/en/

60. Woodside J, Draper J, Lloyd A, et al. Use of biomarkers to assess fruit and vegetable intake. *Proceedings of the Nutrition Society*, 2017, **76**(3), pp.308–315.

61. Aune D, Keum N, Giovannucci E, et al. Dietary intake and blood concentrations of antioxidants and the risk of cardiovascular disease, total cancer, and all-cause mortality: a systematic review and dose-response meta-analysis of prospective studies. *American Journal of Clinical Nutrition*, 2018, **108**(5), pp.1069-1091.

62. Colten HR and Altevogt BM. *Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem.* Washington (DC), 2006.

63. Ancoli-Israel S, Cole R, Alessi C, et al. The role of actigraphy in the study of sleep and circadian rythms. *Sleep*, 2003, **26**(3), pp.342-92.

64. Loomis A, Harvey E and Hobart G. Cerebral states during sleep as studied by human brain potentials *Journal of Experimental Psychology*, 1937, **21**(2), pp.127-144.

65. Dement W and Kleitman N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming. *Electroencephalography and Clinical Neurophysiology: Supplement*, 1957, **9**(4), pp.673-690.

66. Irwin MR. Why sleep is important for health: a psychoneuroimmunology perspective. *Annual Review of Psychology*, 2015, **66**, pp.143-72.

67. Ibanez V, Silva J and Cauli O. A survey on sleep assessment methods. *PeerJ*, 2018, **6**, p.e4849.

68. Martin JL and Hakim AD. Wrist Actigraphy. *Chest*, 2011, **139**(6), pp.1514-1527.

69. Baandrup L and Jennum PJ. A validation of wrist actigraphy against polysomnography in patients with schizophrenia or bipolar disorder. *Neuropsychiatric Disease and Treatment*, 2015, **11**, pp.2271-2277.

70. Kosmadopoulos A, Sargent C, Darwent D, et al. Alternatives to polysomnography (PSG): A validation of wrist actigraphy and a partial-PSG system. *Behavior Research Methods*, 2014, **46**(4), pp.1032-1041.

71. St-Onge MP, Mikic A and Pietrolungo CE. Effects of Diet on Sleep Quality. *Advances in Nutrition*, 2016, **7**(5), pp.938-49.

72. Ogilvie RP and Patel SR. The epidemiology of sleep and obesity. *Sleep Health*, 2017, **3**(5), pp.383-388.

73. Xiang YT, Ma X, Lu JY, et al. Relationships of sleep duration with sleep disturbances, basic socio-demographic factors, and BMI in Chinese people. *Sleep Medicine*, 2009, **10**(10), pp.1085-9.

74. Park S, Cho MJ, Chang SM, et al. Relationships of sleep duration with sociodemographic and health-related factors, psychiatric disorders and sleep disturbances in a community sample of Korean adults. *Journal of Sleep Research*, 2010, **19**(4), pp.567-77.

75. Bin YS. Is Sleep Quality More Important than Sleep Duration for Public Health? *Sleep*, 2016, **39**(9), pp.1629-1630.

76. Roenneberg T, Wirz-Justice A and Merrow M. Life between clocks: Daily temporal patterns of human chronotypes. *Journal of Biological Rhythms*, 2003, **18**(1), pp.80-90.

77. Horne JA and Ostberg O. A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *International Journal of Chronobiology*, 1976, **4**(2), pp.97-110.

78. Gellman MD and Turner JR. *Encyclopedia of Behavioral Medicine.* New York: Springer, 2013.

79. Buysse DJ, Reynolds CF, 3rd, Monk TH, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research*, 1989, **28**(2), pp.193-213.

80. Ibanez V, Silva J and Cauli O. A survey on sleep questionnaires and diaries. *Sleep Medicine*, 2018, **42**, pp.90-96.

81. Jungquist CR, Pender JJ, Klingman KJ, et al. Validation of Capturing Sleep Diary Data via a Wrist-Worn Device. *Sleep Disord*, 2015, **2015**, p.758937.

82. Tonetti L, Mingozzi R and Natale V. Comparison between paper and electronic sleep diary. *Biological Rhythm Research*, 2016, **47**(5), pp.743-753.

83. Girschik J, Fritschi L, Heyworth J, et al. Validation of self-reported sleep against actigraphy. *Journal of Epidemiology*, 2012, **22**(5), pp.462-8.

84. Lauderdale DS, Knutson KL, Yan LL, et al. Self-reported and measured sleep duration: how similar are they? *Epidemiology*, 2008, **19**(6), pp.838-45.

85. Borbély A. A two process model of sleep regulation. *Human Neurobiology*, 1982, **1**(3), pp.195-204.

86. Briguglio M, Dell'osso B, Panzica G, et al. Dietary Neurotransmitters: A Narrative Review on Current Knowledge. *Nutrients*, 2018, **10**(5), p.591.

87. Dong G, Kim YI and Golden SS. Simplicity and complexity in the cyanobacterial circadian clock mechanism. *Current Opinion in Genetics and Development*, 2010, **20**(6), pp.619-25.

88. Potter GD, Cade JE, Grant PJ, et al. Nutrition and the circadian system. *British Journal of Nutrition*, 2016, **116**(3), pp.434-42.

89. Slavin JL and Lloyd B. Health benefits of fruits and vegetables. *Advances in Nutrition*, 2012, **3**(4), pp.506-16.

90. Kamphuis CBM, Giskes K, De Bruijn GJ, et al. Environmental determinants of fruit and vegetable consumption among adults: a systematic review. *British Journal of Nutrition*, 2006, **96**(4), pp.620-635.

91. Guillaumie L, Godin G and Vezina-Im LA. Psychosocial determinants of fruit and vegetable intake in adult population: a systematic review. *The International Journal of Behavioral Nutrition and Physical Activity*, 2010, **7**, p.12.

92. Pollard J, Kirk SF and Cade JE. Factors affecting food choice in relation to fruit and vegetable intake: a review. *Nutrition Research Reviews*, 2002, **15**(2), pp.373-87.

93. Crisp A. Sleep, Activity, Nutrition and Mood. *The British journal of psychiatry: the journal of mental science*, 1980, **137**(1), pp.1-7.

94. Hicks R and Rozette E. Habitual sleep duration and eating disorders in college students. *Perceptual and Motor Skills*, 1986, **62**, pp.209-210.

95. Hicks R, Mctighe S and Juarez M. Sleep duration and eating behaviors of college students. *Perceptual and Motor Skills*, 1986, **62**(1), pp.25-26.

96. Trace SE, Thornton LM, Runfola CD, et al. Sleep problems are associated with binge eating in women. *International Journal of Eating Disorders*, 2012, **45**(5), pp.695-703.

97. Murase K, Tabara Y, Takahashi Y, et al. Gastroesophageal reflux disease symptoms and dietary behaviors are significant correlates of short sleep duration in the general population: the Nagahama Study. *Sleep*, 2014, **37**(11), pp.1809-15.

98. St-Onge MP. The role of sleep duration in the regulation of energy balance: effects on energy intakes and expenditure. *Journal of Clinical Sleep Medicine*, 2013, **9**(1), pp.73-80.

99. Spiegel K, Tasali E, Penev P, et al. Brief communication: Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. *Annals of Internal Medicine*, 2004, **141**(11), pp.846-50.

100. Wells TT and Cruess DG. Effects of partial sleep deprivation on food consumption and food choice. *Psychology & Health*, 2006, **21**(1), pp.79-86.

101. Nedeltcheva AV, Kilkus JM, Imperial J, et al. Sleep curtailment is accompanied by increased intake of calories from snacks. *The American Journal of Clinical Nutrition*, 2009, **89**(1), pp.126-33.

102. Brondel L, Romer MA, Nougues PM, et al. Acute partial sleep deprivation increases food intake in healthy men. *The American Journal of Clinical Nutrition*, 2010, **91**(6), pp.1550-9.

103. Markwald RR, Melanson EL, Smith MR, et al. Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. *Proceedings of the National Academy of Sciences of the United States of America*, 2013, **110**(14), pp.5695-700.

104. Hogenkamp PS, Nilsson E, Nilsson VC, et al. Acute sleep deprivation increases portion size and affects food choice in young men. *Psychoneuroendocrinology*, 2013, **38**(9), pp.1668-74.

105. Spaeth AM, Dinges DF and Goel N. Effects of Experimental Sleep Restriction on Weight Gain, Caloric Intake, and Meal Timing in Healthy Adults. *Sleep*, 2013, **36**(7), pp.981-990.

106. Pardi D, Buman M, Black J, et al. Eating Decisions Based on Alertness Levels After a Single Night of Sleep Manipulation: A Randomized Clinical Trial. *Sleep*, 2017, **40**(2).

107. Capers PL, Fobian AD, Kaiser KA, et al. A systematic review and meta-analysis of randomized controlled trials of the impact of sleep duration on adiposity and components of energy balance. *Obesity Reviews*, 2015, **16**(9), pp.771-82.

108. Al Khatib HK, Harding SV, Darzi J, et al. The effects of partial sleep deprivation on energy balance: a systematic review and meta-analysis. *European Journal of Clinical Nutrition*, 2017, **71**(5), pp.614-624.

109. Shi Z, Mcevoy M, Luu J, et al. Dietary fat and sleep duration in Chinese men and women. *International Journal of Obesity*, 2008, **32**(12), pp.1835-1840.

110. Haghighatdoost F, Karimi G, Esmaillzadeh A, et al. Sleep deprivation is associated with lower diet quality indices and higher rate of general and central obesity among young female students in Iran. *Nutrition*, 2012, **28**(11-12), pp.1146-50.

111. Grandner MA, Jackson N, Gerstner JR, et al. Dietary nutrients associated with short and long sleep duration. Data from a nationally representative sample. *Appetite*, 2013, **64**, pp.71-80.

112. Kant AK and Graubard BI. Association of self-reported sleep duration with eating behaviors of American adults: NHANES 2005-2010. *The American Journal of Clinical Nutrition*, 2014, **100**(3), pp.938-47.

113. Patterson RE, Emond JA, Natarajan L, et al. Short sleep duration is associated with higher energy intake and expenditure among African-American and non-Hispanic white adults. *Journal of Nutrition*, 2014, **144**(4), pp.461-6.

114. Stern JH, Grant AS, Thomson CA, et al. Short sleep duration is associated with decreased serum leptin, increased energy intake and decreased diet quality in postmenopausal women. *Obesity (Silver Spring)*, 2014, **22**(5), pp.E55-61.

115. Grandner MA, Kripke DF, Naidoo N, et al. Relationships among dietary nutrients and subjective sleep, objective sleep, and napping in women. *Sleep Medicine*, 2010, **11**(2), pp.180-4.

116. Galli G, Piaggi P, Mattingly MS, et al. Inverse relationship of food and alcohol intake to sleep measures in obesity. *Nutrition & Diabetes*, 2013, **3**, p.e58.

117. Doo M and Kim Y. Sleep duration and dietary macronutrient consumption can modify the cardiovascular disease for Korean women but not for men. *Lipids in Health and Disease*, 2016, **15**, p.17.

118. Doo M and Kim Y. Association between sleep duration and obesity is modified by dietary macronutrients intake in Korean. *Obesity Research & Clinical Practice*, 2016, **10**(4), pp.424-31.

119. Doo H, Chun H and Doo M. Associations of daily sleep duration and dietary macronutrient consumption with obesity and dyslipidemia in Koreans: A cross-sectional study. *Medicine (Baltimore)*, 2016, **95**(45), p.e5360.

120. Dashti HS, Follis JL, Smith CE, et al. Habitual sleep duration is associated with BMI and macronutrient intake and may be modified by CLOCK genetic variants. *The American Journal of Clinical Nutrition*, 2015, **101**(1), pp.135-43.

121. Dashti HS, Zuurbier LA, De Jonge E, et al. Actigraphic sleep fragmentation, efficiency and duration associate with dietary intake in the Rotterdam Study. *Journal of Sleep Research*, 2016, **25**(4), pp.404-11.

122. Bennett CJ, Truby H, Zia Z, et al. Investigating the relationship between sleep and macronutrient intake in women of childbearing age. *European Journal of Clinical Nutrition*, 2017, **71**(6), pp.712-717.

123. Potter GDM, Cade JE and Hardie LJ. Longer sleep is associated with lower BMI and favorable metabolic profiles in UK adults: Findings from the National Diet and Nutrition Survey. *PloS One*, 2017, **12**(7), p.e0182195.

124. Crispim CA, Zimberg IZ, Dos Reis BG, et al. Relationship between food intake and sleep pattern in healthy individuals. *Journal of Clinical Sleep Medicine*, 2011, **7**(6), pp.659-64.

125. Yamaguchi M, Uemura H, Katsuura-Kamano S, et al. Relationship of dietary factors and habits with sleep-wake regularity. *Asia Pacific Journal of Clinical Nutrition*, 2013, **22**(3), pp.457-65.

126. Cao Y, Taylor AW, Pan X, et al. Dinner fat intake and sleep duration and self-reported sleep parameters over five years: Findings from the Jiangsu Nutrition Study of Chinese adults. *Nutrition*, 2016, **32**(9), pp.970-4.

127. Mavanji V, Billington CJ, Kotz CM, et al. Sleep and obesity: a focus on animal models. *Neuroscience and Biobehavioral Reviews*, 2012, **36**(3), pp.1015-29.

128. Wilkinson K and Shapiro C. Development and validation of the Nonrestorative Sleep Scale (NRSS). *Journal of Clinical Sleep Medicine*, 2013, **9**(9), pp.929-37.

129. Grandner MA, Jackson N, Gerstner JR, et al. Sleep symptoms associated with intake of specific dietary nutrients. *Journal of Sleep Research*, 2014, **23**(1), pp.22-34.

130. Maiani G, Caston MJP, Catasta G, et al. Carotenoids: Actual knowledge on food sources, intakes, stability and bioavailability and their protective role in humans. *Molecular Nutrition & Food Research*, 2009, **53**, pp.S194-S218.

131. Zadeh SS and Begum K. Comparison of nutrient intake by sleep status in selected adults in Mysore, India. *Nutrition Research and Practice*, 2011, **5**(3), pp.230-5.

132. Ji X, Grandner MA and Liu J. The relationship between micronutrient status and sleep patterns: a systematic review. *Public Health Nutrition*, 2017, **20**(4), pp.687-701.

133. Peuhkuri K, Sihvola N and Korpela R. Diet promotes sleep duration and quality. *Nutrition Research*, 2012, **32**(5), pp.309-19.

134. Knowlden AP, Hackman CL and Sharma M. Systematic Review of Dietary Interventions Targeting Sleep Behavior. *Journal of Alternative and Complementary Medicine*, 2016, **22**(5), pp.349-62.

135. Phillips F, Chen CN, Crisp AH, et al. Isocaloric diet changes and electroencephalographic sleep. *Lancet*, 1975, **2**(7938), pp.723-5.

136. Yajima K, Seya T, Iwayama K, et al. Effects of Nutrient Composition of Dinner on Sleep Architecture and Energy Metabolism during Sleep. *Journal of Nutritional Science and Vitaminology*, 2014, **60**(2), pp.114-121.

137. Porter JM and Horne JA. Bed-time food supplements and sleep: effects of different carbohydrate levels. *Electroencephalography and Clinical Neurophysiology*, 1981, **51**(4), pp.426-33.

138. Kwan RM, Thomas S and Mir MA. Effects of a low carbohydrate isoenergetic diet on sleep behavior and pulmonary functions in healthy female adult humans. *Journal of Nutrition*, 1986, **116**(12), pp.2393-402.

139. Wells A, Read N, Idzikowski C, et al. Effects of meals on objective and subjective measures of daytime sleepiness. *Journal of Applied Physiology*, 1998, **84**(2), pp.507-15.

140. Afaghi A, O'connor H and Chow CM. High-glycemic-index carbohydrate meals shorten sleep onset. *The American Journal of Clinical Nutrition*, 2007, **85**(2), pp.426-30.

141. Afaghi A, O'connor H and Chow C. Acute effects of the very low carbohydrate diet on sleep indices. *Nutritional Neuroscience*, 2008, **11**(4), pp.146-54.

142. Lindseth G, Lindseth P and Thompson M. Nutritional effects on sleep. *Western Journal of Nursing Research*, 2013, **35**(4), pp.497-513.

143. Lindseth G and Murray A. Dietary Macronutrients and Sleep. *Western Journal of Nursing Research*, 2016, **38**(8), pp.938-58.

144. Hartmann E. Effects of L-tryptophan on sleepiness and on sleep. *Journal of Psychiatric Research*, 1982, **17**(2), pp.107-13.

145. Silber BY and Schmitt JA. Effects of tryptophan loading on human cognition, mood, and sleep. *Neuroscience and Biobehavioral Reviews*, 2010, **34**(3), pp.387-407.

146. Espana RA and Scammell TE. Sleep neurobiology from a clinical perspective. *Sleep*, 2011, **34**(7), pp.845-58.

147. Jones BE. Neurobiology of waking and sleeping. *Handbook of Clinical Neurology*, 2011, **98**, pp.131-49.

148. Wells AS, Read NW, Uvnas-Moberg K, et al. Influences of fat and carbohydrate on postprandial sleepiness, mood, and hormones. *Physiology and Behavior*, 1997, **61**(5), pp.679-86.

149. Koliaki C, Kokkinos A, Tentolouris N, et al. The effect of ingested macronutrients on postprandial ghrelin response: a critical review of existing literature data. *International journal of peptides*, 2010, **2010**, p.710852.

150. Shrestha YB, Wickwire K and Giraudo SQ. Direct effects of nutrients, acetylcholine, CCK, and insulin on ghrelin release from the isolated stomachs of rats. *Peptides*, 2009, **30**(6), pp.1187-91.

151. Nakahara K, Okame R, Katayama T, et al. Nutritional and environmental factors affecting plasma ghrelin and leptin levels in rats. *Journal of Endocrinology*, 2010, **207**(1), pp.95-103.

152. Steiger A. Neurochemical regulation of sleep. *Journal of Psychiatric Research*, 2007, **41**(7), pp.537-52.

153. Steiger A, Dresler M, Schussler P, et al. Ghrelin in mental health, sleep, memory. *Molecular and Cellular Endocrinology*, 2011, **340**(1), pp.88-96.

154. Garcia-Garcia F, Juarez-Aguilar E, Santiago-Garcia J, et al. Ghrelin and its interactions with growth hormone, leptin and orexins: implications for the sleep-wake cycle and metabolism. *Sleep Medicine Reviews*, 2014, **18**(1), pp.89-97.

155. Kluge M, Schussler P, Zuber V, et al. Ghrelin administered in the early morning increases secretion of cortisol and growth hormone without affecting sleep. *Psychoneuroendocrinology*, 2007, **32**(3), pp.287-292.

156. Schussler P, Uhr M, Ising M, et al. Nocturnal ghrelin, ACTH, GH and cortisol secretion after sleep deprivation in humans. *Psychoneuroendocrinology*, 2006, **31**(8), pp.915-23.

157. Akanmu M, Ukponmwan O, Katayama Y, et al. Neuropeptide-Y Y2-receptor agonist, PYY3-36 promotes non–rapid eye movement sleep in rat. *Neuroscience Research*, 2006, **54**(3).

158. Hagan MM and Moss DE. Effect of naloxone and antidepressants on hyperphagia produced by peptide YY. *Pharmacology, Biochemistry and Behavior*, 1993, **45**(4), pp.941-4.

159. Friedman M. Analysis, Nutrition, and Health Benefits of Tryptophan. *International Journal of Tryptophan Research*, 2018, **11**, pp.1-12.

160. Wheatley D. Medicinal plants for insomnia: a review of their pharmacology, efficacy and tolerability. *Journal of Psychopharmacology*, 2005, **19**(4), pp.414-21.

161. Sanchez-Ortuno MM, Belanger L, Ivers H, et al. The use of natural products for sleep: A common practice? *Sleep Medicine*, 2009, **10**(9), pp.982-7.

162. Meolie AL, Rosen C, Kristo D, et al. Oral nonprescription treatment for insomnia: an evaluation of products with limited evidence. *Journal of Clinical Sleep Medicine*, 2005, **1**(2), pp.173-87.

163. Southwell PR, Evans CR and Hunt JN. Effect of a hot milk drink on movements during sleep. *British Medical Journal*, 1972, **2**(5811), pp.429-31.

164. Brezinova V and Oswald I. Sleep after a bedtime beverage. *British Medical Journal*, 1972, **2**(5811), pp.431-3.

165. Adam K. Dietary habits and sleep after bedtime food drinks. *Sleep*, 1980, **3**(1), pp.47-58.

166. Valtonen M, Niskanen L, Kangas AP, et al. Effect of melatonin-rich night-time milk on sleep and activity in elderly institutionalized subjects. *Nord J Psychiatry*, 2005, **59**(3), pp.217-21.

167. Yamamura S, Morishima H, Kumano-Go T, et al. The effect of Lactobacillus helveticus fermented milk on sleep and health perception in elderly subjects. *European Journal of Clinical Nutrition*, 2009, **63**(1), pp.100-5.

168. Hansen AL, Dahl L, Olson G, et al. Fish consumption, sleep, daily functioning, and heart rate variability. *Journal of Clinical Sleep Medicine*, 2014, **10**(5), pp.567-75.

169. Del Brutto OH, Mera RM, Ha JE, et al. Dietary fish intake and sleep quality: a population-based study. *Sleep Medicine*, 2016, **17**, pp.126-8.

170. St-Onge MP, Roberts A, Shechter A, et al. Fiber and Saturated Fat Are Associated with Sleep Arousals and Slow Wave Sleep. *Journal of Clinical Sleep Medicine*, 2016, **12**(1), pp.19-24.

171. Garaulet M, Ortega FB, Ruiz JR, et al. Short sleep duration is associated with increased obesity markers in European adolescents: effect of physical activity and dietary habits. The HELENA study. *International Journal of Obesity (2005)*, 2011, **35**(10), pp.1308-17.

172. Golley R, Maher C, Matricciani L, et al. Sleep duration or bedtime? Exploring the association between sleep timing behaviour, diet and BMI in children and adolescents. *International Journal of Obesity (2005)*, 2013, **37**(4), pp.546-551.

173. Hoppe C, Rothausen BW, Biltoft-Jensen A, et al. Relationship between sleep duration and dietary intake in 4- to 14-year-old Danish children. *Journal of Nutritional Science*, 2013, **2**(e38), pp.1-7.

174. Beebe DW, Simon S, Summer S, et al. Dietary intake following experimentally restricted sleep in adolescents. *Sleep*, 2013, **36**(6), pp.827-34.

175. Franckle RL, Falbe J, Gortmaker S, et al. Insufficient sleep among elementary and middle school students is linked with elevated soda consumption and other unhealthy dietary behaviors. *Preventive Medicine*, 2015, **74**, pp.36-41.

176. Bornhorst C, Wijnhoven TM, Kunesova M, et al. WHO European Childhood Obesity Surveillance Initiative: associations between sleep duration, screen time and food consumption frequencies. *BMC Public Health*, 2015, **15**, p.442.

177. Cao M, Zhu Y, He B, et al. Association between sleep duration and obesity is age- and gender-dependent in Chinese urban children aged 6–18 years: a cross-sectional study. *BMC Public Health*, 2015, **15**(1).

178. Arora T and Taheri S. Associations among late chronotype, body mass index and dietary behaviors in young adolescents. *International Journal of Obesity (2005)*, 2015, **39**(1), pp.39-44.

179. Ferranti R, Marventano S, Castellano S, et al. Sleep quality and duration is related with diet and obesity in young adolescent living in Sicily, Southern Italy. *Sleep Science*, 2016, **9**(2), pp.117-22.

180. Khan MKA, Faught EL, Chu YL, et al. Is it nutrients, food items, diet quality or eating behaviours that are responsible for the association of children's diet with sleep? *Journal of Sleep Research*, 2017, **26**(4), pp.468-476.

181. Asarnow LD, Greer SM, Walker MP, et al. The Impact of Sleep Improvement on Food Choices in Adolescents With Late Bedtimes. *Journal of Adolescent Health*, 2017, **60**(5), pp.570-576.

182. Gong QH, Li H, Zhang XH, et al. Associations between sleep duration and physical activity and dietary behaviors in Chinese adolescents: results from the Youth Behavioral Risk Factor Surveys of 2015. *Sleep Medicine*, 2017, **37**, pp.168-173.

183. Harrex HaL, Skeaff SA, Black KE, et al. Sleep timing is associated with diet and physical activity levels in 9-11-year-old children from Dunedin, New Zealand: the PEDALS study. *Journal of Sleep Research*, 2018, **27**(4), p.e12634.

184. Kaar JL, Schmiege SJ, Vadiveloo M, et al. Sleep duration mediates the relationship between health behavior patterns and obesity. *Sleep Health*, 2018, **4**(5), pp.442-447.

185. Cordova FV, Barja S and Brockmann PE. Consequences of short sleep duration on the dietary intake in children: A systematic review and metanalysis. *Sleep Medicine Reviews*, 2018, **42**, pp.68-84.

186. Imaki M, Hatanaka Y, Ogawa Y, et al. An epidemiological study on relationship between the hours of sleep and life style factors in japanese factory workers. *Journal of Physiological Anthropology and Applied Human Science*, 2002, **21**(2), pp.115-120.

187. Huang YC, Wahlqvist ML and Lee MS. Sleep quality in the survival of elderly taiwanese: roles for dietary diversity and pyridoxine in men and women. *Journal of the American College of Nutrition*, 2013, **32**(6), pp.417-27.

188. Heath G, Roach GD, Dorrian J, et al. The effect of sleep restriction on snacking behaviour during a week of simulated shiftwork. *Accident Analysis and Prevention*, 2012, **45 Suppl**, pp.62-7.

189. Spaeth AM, Dinges DF and Goel N. Sex and race differences in caloric intake during sleep restriction in healthy adults. *The American Journal of Clinical Nutrition*, 2014, **100**(2), pp.559-66.

190. Tasali E, Chapotot F, Wroblewski K, et al. The effects of extended bedtimes on sleep duration and food desire in overweight young adults: a home-based intervention. *Appetite*, 2014, **80**, pp.220-4.

191. Garrido M, Espino J, González-Gómez D, et al. A nutraceutical product based on Jerte Valley cherries improves sleep and augments the antioxidant status in humans. *e-SPEN, the European E-Journal of Clinical Nutrition and Metabolism*, 2009, **4**(6), pp.e321-e323.

192. Garrido M, Paredes SD, Cubero J, et al. Jerte Valley cherry-enriched diets improve nocturnal rest and increase 6-sulfatoxymelatonin and total antioxidant capacity in the urine of middle-aged and elderly humans. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 2010, **65**(9), pp.909-14.

193. Pigeon W, Carr M, Gorman C, et al. Effects of a Tart Cherry Juice Beverage on the Sleep of Older Adults with Insomnia: A Pilot Study. *Journal of Medicinal Food*, 2010, **13**(3), pp.579-583.

194. Lin H, Tsai P, Fang S, et al. Effect of kiwifruit consumption on sleep quality in adults with sleep problems. *Asia Pacific Journal of Clinical Nutrition*, 2011, **20**(2), pp.169-74.

195. Howatson G, Bell PG, Tallent J, et al. Effect of tart cherry juice (Prunus cerasus) on melatonin levels and enhanced sleep quality. *European Journal of Nutrition*, 2012, **51**(8), pp.909-16.

196. Garrido M, González-Gómez D, Lozano M, et al. A jerte valley cherry product provides beneficial effects on sleep quality. Influence on aging. *The Journal of Nutrition, Health & Aging*, 2013, **17**(6), pp.553-60.

197. Patterson F, Malone SK, Lozano A, et al. Smoking, Screen-Based Sedentary Behavior, and Diet Associated with Habitual Sleep Duration and Chronotype: Data from the UK Biobank. *Annals of Behavioral Medicine*, 2016, **50**(5), pp.715-726.

198. Patterson F, Malone SK, Grandner MA, et al. Interactive effects of sleep duration and morning/evening preference on cardiovascular risk factors. *European Journal of Public Health*, 2018, **28**(1), pp.155-161.

199. Duke CH, Williamson JA, Snook KR, et al. Association Between Fruit and Vegetable Consumption and Sleep Quantity in Pregnant Women. *Maternal and Child Health Journal*, 2017, **21**(5), pp.966-973.

200. Lee YH, Chang YC, Lee YT, et al. Dietary patterns with fresh fruits and vegetables consumption and quality of sleep among older adults in mainland China. *Sleep and Biological Rhythms*, 2018, **16**(3), pp.293-305.

201. Stamatakis KA and Brownson RC. Sleep duration and obesity-related risk factors in the rural Midwest. *Preventive Medicine*, 2008, **46**(5), pp.439-44.

202. Patel SR, Malhotra A, White DP, et al. Association between reduced sleep and weight gain in women. *American Journal of Epidemiology*, 2006, **164**(10), pp.947-54.

203. Tu X, Cai H, Gao YT, et al. Sleep duration and its correlates in middle-aged and elderly Chinese women: the Shanghai Women's Health Study. *Sleep Medicine*, 2012, **13**(9), pp.1138-45.

204. Mota MC, Waterhouse J, De-Souza DA, et al. Sleep pattern is associated with adipokine levels and nutritional markers in resident physicians. *Chronobiology International*, 2014, **31**(10), pp.1130-8.

205. Mossavar-Rahmani Y, Jung M, Patel SR, et al. Eating behavior by sleep duration in the Hispanic Community Health Study/Study of Latinos. *Appetite*, 2015, **95**, pp.275-84.

206. Van Lee L, Chia AR, Loy SL, et al. Sleep and Dietary Patterns in Pregnancy: Findings from the GUSTO Cohort. *International Journal of Environmental Research and Public Health*, 2017, **14**(11).

207. Adams TB and Colner W. The association of multiple risk factors with fruit and vegetable intake among a nationwide sample of college students. *Journal of American College Health*, 2008, **56**(4), pp.455-61.

208. Buxton OM, Quintiliani LM, Yang MH, et al. Association of sleep adequacy with more healthful food choices and positive workplace experiences among motor freight workers. *American Journal of Public Health*, 2009, **99 Suppl 3**, pp.S636-43.

209. Baron KG, Reid KJ, Kern AS, et al. Role of sleep timing in caloric intake and BMI. *Obesity (Silver Spring)*, 2011, **19**(7), pp.1374-81.

210. Kim S, Deroo LA and Sandler DP. Eating patterns and nutritional characteristics associated with sleep duration. *Public Health Nutrition*, 2011, **14**(5), pp.889-95.

211. Mosca M and Aggarwal B. Sleep duration, snoring habits, and cardiovascular disease risk factors in an ethnically diverse population. *Journal of Cardiovascular Nursing*, 2012, **27**(3), pp.263-9.

212. Chang MW, Brown R, Nitzke S, et al. Stress, sleep, depression and dietary intakes among low-income overweight and obese pregnant women. *Maternernal and Child Health Journal*, 2015, **19**(5), pp.1047-59.

213. Silva CM, Mota MC, Miranda MT, et al. Chronotype, social jetlag and sleep debt are associated with dietary intake among Brazilian undergraduate students. *Chronobiology International*, 2016, **33**(6), pp.740-8.

214. Xiao RS, Moore Simas TA, Pagoto SL, et al. Sleep Duration and Diet Quality Among Women Within 5 Years of Childbirth in the United States: A Cross-Sectional Study. *Maternernal and Child Health Journal*, 2016, **20**(9), pp.1869-77.

215. Doo M and Kim Y. The Risk of Being Obese According to Short Sleep Duration Is Modulated after Menopause in Korean Women. *Nutrients*, 2017, **9**(3).

216. Kleiser C, Wawro N, Stelmach-Mardas M, et al. Are sleep duration, midpoint of sleep and sleep quality associated with dietary intake among Bavarian adults? *European Journal of Clinical Nutrition*, 2017, **71**(5), pp.631-637.

217. Mossavar-Rahmani Y, Weng J, Wang R, et al. Actigraphic sleep measures and diet quality in the Hispanic Community Health Study/Study of Latinos Sueno ancillary study. *Journal of Sleep Research*, 2017, **26**(6), pp.739-746.

218. Timmermans M, Mackenbach JD, Charreire H, et al. Exploring the mediating role of energy balance-related behaviours in the association between sleep duration and obesity in European adults. The SPOTLIGHT project. *Preventive Medicine*, 2017, **100**, pp.25-32.

219. Gebski J, Jezewska-Zychowicz M, Guzek D, et al. The Associations between Dietary Patterns and Short Sleep Duration in Polish Adults (LifeStyle Study). *International Journal of Environmental Research and Public Health*, 2018, **15**(11), p.2497.

220. Peltzer K and Pengpid S. Self-Reported Sleep Duration and Its Correlates with Sociodemographics, Health Behaviours, Poor Mental Health, and Chronic Conditions in Rural Persons 40 Years and Older in South Africa. *International Journal of Environmental Research and Public Health*, 2018, **15**(7), p.1357.

221. Tan SL, Storm V, Reinwand DA, et al. Understanding the Positive Associations of Sleep, Physical Activity, Fruit and Vegetable Intake as Predictors of Quality of Life and Subjective Health Across Age Groups: A Theory Based, Cross-Sectional Web-Based Study. *Frontiers in Psychology*, 2018, **9**, p.977.

222. Vezina-Im LA, Lebel A, Gagnon P, et al. Individual Correlates of Sleep Among Childbearing Age Women in Canada. *Behavioral Sleep Medicine*, 2018, pp.1-12.

223. Vezina-Im LA, Lebel A, Gagnon P, et al. Association between sleep and overweight/obesity among women of childbearing age in Canada. *Canadian Journal of Public Health. Revue Canadienne de Santé Publique*, 2018, **109**(4), pp.516-526.

224. Hoefelmann LP, Lopes Ada S, Silva KS, et al. Lifestyle, self-reported morbidities, and poor sleep quality among Brazilian workers. *Sleep Medicine*, 2012, **13**(9), pp.1198-201.

225. Beydoun MA, Gamaldo AA, Canas JA, et al. Serum nutritional biomarkers and their associations with sleep among US adults in recent national surveys. *PloS One*, 2014, **9**(8), p.e103490.

226. Katagiri R, Asakura K, Kobayashi S, et al. Low Intake of Vegetables, High Intake of Confectionary, and Unhealthy Eating Habits are Associated with Poor Sleep Quality among Middle-aged Female Japanese Workers. *Journal of Occupational Health*, 2014, **56**(5), pp.359-368.

227. Grandner MA, Jackson NJ, Izci-Balserak B, et al. Social and Behavioral Determinants of Perceived Insufficient Sleep. *Frontiers in Neurology*, 2015, **6**, p.112.

228. Kurotani K, Kochi T, Nanri A, et al. Dietary patterns and sleep symptoms in Japanese workers: the Furukawa Nutrition and Health Study. *Sleep Medicine*, 2015, **16**(2), pp.298-304.

229. Quick V, Byrd-Bredbenner C, Shoff S, et al. Relationships of Sleep Duration With Weight-Related Behaviors of U.S. College Students. *Behavioral Sleep Medicine*, 2016, **14**(5), pp.565-80.

230. Perez-Rodrigo C, Gianzo-Citores M, Gil A, et al. Lifestyle Patterns and Weight Status in Spanish Adults: The ANIBES Study. *Nutrients*, 2017, **9**(6).

231. Wang S, Wu Y, Ungvari GS, et al. Sleep duration and its association with demographics, lifestyle factors, poor mental health and chronic diseases in older Chinese adults. *Psychiatry Research*, 2017, **257**, pp.212-218.

232. Altman DG and Bland JM. Measurement in Medicine - the Analysis of Method Comparison Studies. *Journal of the Royal Statistical Society. Series D (The Statistician)*, 1983, **32**(3), pp.307-317.

233. Almoosawi S, Vingeliene S, Gachon F, et al. Chronotype: Implications for Epidemiologic Studies on Chrono-Nutrition and Cardiometabolic Health. *Advances in Nutrition*, 2019, **10**(1), pp.30-42.

234. Von Schantz M. Phenotypic effects of genetic variability in human clock genes on circadian and sleep parameters. *Journal of Genetics*, 2008, **87**(5), pp.513-9.

235. Jones CR, Campbell SS, Zone SE, et al. Familial advanced sleep-phase syndrome: A short-period circadian rhythm variant in humans. *Nature Medicine*, 1999, **5**(9), pp.1062-5.

236. Smith MR, Burgess HJ, Fogg LF, et al. Racial differences in the human endogenous circadian period. *PloS One*, 2009, **4**(6), p.e6014.

237. Lehnkering H and Siegmund R. Influence of chronotype, season, and sex of subject on sleep behavior of young adults. *Chronobiology International*, 2007, **24**(5), pp.875-88.

238. Roenneberg T, Allebrandt KV, Merrow M, et al. Social jetlag and obesity. *Current Biology*, 2012, **22**(10), pp.939-43.

239. Adan A. Chronotype and personality factors in the daily consumption of alcohol and psychostimulants. *Addiction*, 1994, **89**(4), pp.455-62.

240. Reutrakul S and Knutson KL. Consequences of Circadian Disruption on Cardiometabolic Health. *Sleep Medicine Clinics*, 2015, **10**(4), pp.455-68.

241. Merikanto I, Lahti T, Puolijoki H, et al. Associations of chronotype and sleep with cardiovascular diseases and type 2 diabetes. *Chronobiology International*, 2013, **30**(4), pp.470-7.

242. Yu JH, Yun CH, Ahn JH, et al. Evening Chronotype Is Associated With Metabolic Disorders and Body Composition in Middle-Aged Adults. *Journal of Clinical Endocrinology and Metabolism*, 2015, **100**(4), pp.1494-1502.

243. Melo MCA, Abreu RLC, Linhares Neto VB, et al. Chronotype and circadian rhythm in bipolar disorder: A systematic review. *Sleep Medicine Reviews*, 2017, **34**, pp.46-58.

244. Knutson KL and Von Schantz M. Associations between chronotype, morbidity and mortality in the UK Biobank cohort. *Chronobiology International*, 2018, **35**(8), pp.1045-1053.

245. Malone SK, Zemel B, Compher C, et al. Characteristics Associated with Sleep Duration, Chronotype, and Social Jet Lag in Adolescents. *Journal of School Nursing*, 2016, **32**(2), pp.120-31.

246. Sato-Mito N, Shibata S, Sasaki S, et al. Dietary intake is associated with human chronotype as assessed by both morningness-eveningness score and preferred midpoint of sleep in young Japanese women. *International Journal of Food Sciences and Nutrition*, 2011, **62**(5), pp.525-32.

247. Sato-Mito N, Sasaki S, Murakami K, et al. The midpoint of sleep is associated with dietary intake and dietary behavior among young Japanese women. *Sleep Medicine*, 2011, **12**(3), pp.289-94.

248. Yoshizaki T, Komatsu T, Tada Y, et al. Association of habitual dietary intake with morningness-eveningness and rotating shift work in Japanese female nurses. *Chronobiology International*, 2018, **35**(3), pp.392-404.

249. Kanerva N, Kronholm E, Partonen T, et al. Tendency toward eveningness is associated with unhealthy dietary habits. *Chronobiology International*, 2012, **29**(7), pp.920-7.

250. Fleig D and Randler C. Association between chronotype and diet in adolescents based on food logs. *Eating Behaviors*, 2009, **10**(2), pp.115-8.

251. Mota MC, Waterhouse J, De-Souza DA, et al. Association between chronotype, food intake and physical activity in medical residents. *Chronobiology International*, 2016, **33**(6), pp.730-9.

252. Knutson KL, Spiegel K, Penev P, et al. The metabolic consequences of sleep deprivation. *Sleep Medicine Reviews*, 2007, **11**(3), pp.163-78.

253. Patel SR and Hu FB. Short sleep duration and weight gain: a systematic review. *Obesity (Silver Spring)*, 2008, **16**(3), pp.643-53.

254. Chaput J-P and Tremblay A. Insufficient Sleep as a Contributor to Weight Gain: An Update. *Current Obesity Reports*, 2012, **1**(4), pp.245-256.

255. Chaput JP. Sleep patterns, diet quality and energy balance. *Physiology and Behavior*, 2014, **134**, pp.86-91.

256. Lundahl A and Nelson TD. Sleep and food intake: A multisystem review of mechanisms in children and adults. *Journal of Health Psychology*, 2015, **20**(6), pp.794-805.

257. Bayon V, Leger D, Gomez-Merino D, et al. Sleep debt and obesity. *Annals of Medicine*, 2014, **46**(5), pp.264-72.

258. Klok MD, Jakobsdottir S and Drent ML. The role of leptin and ghrelin in the regulation of food intake and body weight in humans: a review. *Obesity Reviews*, 2007, **8**(1), pp.21-34.

259. Mullington J, Chan J, Van Dongen H, et al. Sleep Loss Reduces Diurnal Rhythm Amplitude of Leptin in Healthy Men. *Journal of Neuroendocrinology*, 2003, **15**(9), pp.851-854.

260. Spiegel K, Leproult R, L'hermite-Baleriaux M, et al. Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin. *Journal of Clinical Endocrinology and Metabolism*, 2004, **89**(11), pp.5762-71.

261. Schmid SM, Hallschmid M, Jauch-Chara K, et al. A single night of sleep deprivation increases ghrelin levels and feelings of hunger in normal-weight healthy men. *Journal of Sleep Research*, 2008, **17**(3), pp.331-4.

262. Hart CN, Carskadon MA, Considine RV, et al. Changes in Children's Sleep Duration on Food Intake, Weight, and Leptin. *Pediatrics*, 2013, **132**(6), p.e1478.

263. Broussard JL, Kilkus JM, Delebecque F, et al. Elevated ghrelin predicts food intake during experimental sleep restriction. *Obesity (Silver Spring)*, 2016, **24**(1), pp.132-8.

264. Spiegel K, Leproult R and Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet*, 1999, **354**(9188), pp.1435-9.

265. Pejovic S, Vgontzas AN, Basta M, et al. Leptin and hunger levels in young healthy adults after one night of sleep loss. *Journal of Sleep Research*, 2010, **19**(4), pp.552-8.

266. Calvin AD, Carter RE, Adachi T, et al. Effects of experimental sleep restriction on caloric intake and activity energy expenditure. *Chest*, 2013, **144**(1), pp.79-86.

267. Taheri S, Lin L, Austin D, et al. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. *PLoS Medicine*, 2004, **1**(3), p.e62.

268. St-Onge MP. Impact of sleep duration on food intake regulation: Different mechanisms by sex? *Obesity (Silver Spring)*, 2016, **24**(1), p.11.

269. Chaput JP and St-Onge MP. Increased food intake by insufficient sleep in humans: are we jumping the gun on the hormonal explanation? *Frontiers in Endocrinology*, 2014, **5**, p.116.

270. Chapman CD, Benedict C, Brooks SJ, et al. Lifestyle determinants of the drive to eat: a meta-analysis. *The American Journal of Clinical Nutrition*, 2012, **96**(3), pp.492-7.

271. Greer SM, Goldstein AN and Walker MP. The impact of sleep deprivation on food desire in the human brain. *Nature Communications*, 2013, **4**, p.2259.

272. Chapman CD, Nilsson EK, Nilsson VC, et al. Acute sleep deprivation increases food purchasing in men. *Obesity (Silver Spring)*, 2013, **21**(12), pp.E555-60.

273. Tan X, Chapman CD, Cedernaes J, et al. Association between long sleep duration and increased risk of obesity and type 2 diabetes: A review of possible mechanisms. *Sleep Medicine Reviews*, 2018, **40**, pp.127-134.

274. Lutter M and Nestler EJ. Homeostatic and hedonic signals interact in the regulation of food intake. *Journal of Nutrition*, 2009, **139**(3), pp.629-32.

275. Chaput JP. Short sleep duration promoting overconsumption of food: A reward-driven eating behavior? *Sleep*, 2010, **33**(9), pp.1135-6.

276. Benedict C, Brooks SJ, O'daly OG, et al. Acute sleep deprivation enhances the brain's response to hedonic food stimuli: an fMRI study. *Journal of Clinical Endocrinology and Metabolism*, 2012, **97**(3), pp.E443-7.

277. St-Onge MP, Mcreynolds A, Trivedi ZB, et al. Sleep restriction leads to increased activation of brain regions sensitive to food stimuli. *The American Journal of Clinical Nutrition*, 2012, **95**(4), pp.818-24.

278. Killgore WD, Schwab ZJ, Weber M, et al. Daytime sleepiness affects prefrontal regulation of food intake. *Neuroimage*, 2013, **71**, pp.216-23.

279. St-Onge MP, Wolfe S, Sy M, et al. Sleep restriction increases the neuronal response to unhealthy food in normal-weight individuals. *International Journal of Obesity (2005)*, 2014, **38**(3), pp.411-6.

280. Mcneil J, Forest G, Hintze LJ, et al. The effects of partial sleep restriction and altered sleep timing on appetite and food reward. *Appetite*, 2017, **109**, pp.48-56.

281. Hays NP and Roberts SB. Aspects of eating behaviors "disinhibition" and "restraint" are related to weight gain and BMI in women. *Obesity (Silver Spring)*, 2008, **16**(1), pp.52-8.

282. Kelly NR, Shomaker LB, Radin RM, et al. Associations of sleep duration and quality with disinhibited eating behaviors in adolescent girls at-risk for type 2 diabetes. *Eating Behaviors*, 2016, **22**, pp.149-155.

283. Blumfield ML, Bei B, Zimberg IZ, et al. Dietary disinhibition mediates the relationship between poor sleep quality and body weight. *Appetite*, 2018, **120**, pp.602-608.

284. Chaput JP, Després JP, Bouchard C, et al. The Association between Short Sleep Duration and Weight Gain is Dependent on Disinhibited eating Behavior in Adults. *Sleep*, 2011, **34**(10), pp.1291-1297.

285. Bryant EJ, King NA and Blundell JE. Disinhibition: its effects on appetite and weight regulation. *Obesity Reviews*, 2008, **9**(5), pp.409-419.

286. Contento IR, Zybert P and Williams SS. Relationship of cognitive restraint of eating and disinhibition to the quality of food choices of Latina women and their young children. *Preventive Medicine*, 2005, **40**(3), pp.326-336.

287. Borg P, Fogelholm M and Kukkonen-Harjula K. Food selection and eating behaviour during weight maintenance intervention and 2-y follow-up in obese men. *International Journal of Obesity*, 2004, **28**(12), pp.1548-1554.

288. Dweck JS, Jenkins SM and Nolan LJ. The role of emotional eating and stress in the influence of short sleep on food consumption. *Appetite*, 2014, **72**, pp.106-13.

289. Beattie L, Kyle SD, Espie CA, et al. Social interactions, emotion and sleep: A systematic review and research agenda. *Sleep Medicine Reviews*, 2015, **24**, pp.83-100.

290. Gibson EL. Emotional influences on food choice: sensory, physiological and psychological pathways. *Physiology and Behavior*, 2006, **89**(1), pp.53-61.

291. Rossa KR, Smith SS, Allan AC, et al. The effects of sleep restriction on executive inhibitory control and affect in young adults. *Journal of Adolescent Health*, 2014, **55**(2), pp.287-92.

292. Swinburn B and Egger G. Preventive strategies against weight gain and obesity. *Obesity Reviews*, 2002, **3**(4), pp.289-301.

293. Khurana S, Venkataraman K, Hollingsworth A, et al. Polyphenols: benefits to the cardiovascular system in health and in aging. *Nutrients*, 2013, **5**(10), pp.3779-827.

294. Du G, Sun L, Zhao R, et al. Polyphenols: Potential source of drugs for the treatment of ischaemic heart disease. *Pharmacology and Therapeutics*, 2016, **162**, pp.23-34.

295. Tressera-Rimbau A, Arranz S, Eder M, et al. Dietary Polyphenols in the Prevention of Stroke. *Oxidative Medicine and Cellular Longevity*, 2017, **2017**, p.7467962.

296. Zhou Y, Zheng J, Li Y, et al. Natural Polyphenols for Prevention and Treatment of Cancer. *Nutrients*, 2016, **8**(8), p.515.

297. Manach C, Scalbert A, Morand C, et al. Polyphenols: food sources and bioavailability. *The American Journal of Clinical Nutrition*, 2004, **79**(5), pp.727-47.

298. Rendeiro C, Rhodes JS and Spencer JPE. The mechanisms of action of flavonoids in the brain: Direct versus indirect effects. *Neurochemistry International*, 2015, **89**, pp.126-39.

299. Rasch B and Born J. About sleep's role in memory. *Physiological Reviews*, 2013, **93**(2), pp.681–766.

300. Wang LE, Cui XY, Cui SY, et al. Potentiating effect of spinosin, a C-glycoside flavonoid of Semen Ziziphi spinosae, on pentobarbital-induced sleep may be related to postsynaptic 5-HT(1A) receptors. *Phytomedicine*, 2010, **17**(6), pp.404-9.

301. Cho S, Yang H, Jeon YJ, et al. Phlorotannins of the edible brown seaweed Ecklonia cava Kjellman induce sleep via positive allosteric modulation of gamma-aminobutyric acid type A-benzodiazepine receptor: A novel neurological activity of seaweed polyphenols. *Food Chemistry*, 2012, **132**(3), pp.1133-1142.

302. Cho S, Yoon M, Pae AN, et al. Marine polyphenol phlorotannins promote non-rapid eye movement sleep in mice via the benzodiazepine site of the GABAA receptor. *Psychopharmacology*, 2014, **231**(14), pp.2825-37.

303. Shrestha S, Park JH, Lee DY, et al. Rhus parviflora and its biflavonoid constituent, rhusflavone, induce sleep through the positive allosteric modulation of GABA(A)-benzodiazepine receptors. *Journal of Ethnopharmacology*, 2012, **142**(1), pp.213-20.

304. Yang H, Lee YC, Han KS, et al. Green and gold kiwifruit peel ethanol extracts potentiate pentobarbital-induced sleep in mice via a GABAergic mechanism. *Food Chemistry*, 2013, **136**(1), pp.160-3.

305. Zhao W, Li Y, Ma W, et al. A study on quality components and sleep-promoting effects of GABA black tea. *Food & Function*, 2015, **6**(10), pp.3393-8.

306. Delgado J, Terron MP, Garrido M, et al. Diets enriched with a Jerte Valley cherry-based nutraceutical product reinforce nocturnal behaviour in young and old animals of nocturnal (Rattus norvegicus) and diurnal (Streptopelia risoria) chronotypes. *Journal of Animal Physiology and Animal Nutrition*, 2013, **97**(1), pp.137-45.

307. Pifferi F, Dal-Pan A, Menaker M, et al. Resveratrol dietary supplementation shortens the free-running circadian period and decreases body temperature in a prosimian primate. *Journal of Biological Rhythms*, 2011, **26**(3), pp.271-5.

308. Pifferi F, Dal-Pan A, Languille S, et al. Effects of resveratrol on daily rhythms of locomotor activity and body temperature in young and aged grey mouse lemurs. *Oxidative Medicine and Cellular Longevity*, 2013, **2013**, p.187301.

309. Ribas-Latre A, Del Bas JM, Baselga-Escudero L, et al. Dietary proanthocyanidins modulate melatonin levels in plasma and the expression pattern of clock genes in the hypothalamus of rats. *Molecular Nutrition & Food Research*, 2015, **59**(5), pp.865-78.

310. Oike H and Kobori M. Resveratrol Regulates Circadian Clock Genes in Rat-1 Fibroblast Cells. *Bioscience, Biotechnology, and Biochemistry*, 2014, **72**(11), pp.3038-3040.

311. Miranda J, Portillo MP, Madrid JA, et al. Effects of resveratrol on changes induced by high-fat feeding on clock genes in rats. *British Journal of Nutrition*, 2013, **110**(8), pp.1421-8.

312. Ribas-Latre A, Baselga-Escudero L, Casanova E, et al. Chronic consumption of dietary proanthocyanidins modulates peripheral clocks in healthy and obese rats. *The Journal of Nutritional Biochemistry*, 2015, **26**(2), pp.112-9.

313. Ribas-Latre A, Baselga-Escudero L, Casanova E, et al. Dietary proanthocyanidins modulate BMAL1 acetylation, Nampt expression and NAD levels in rat liver. *Scientific Reports*, 2015, **5**, p.10954.

314. Yoon M and Cho S. Triphlorethol A, a Dietary Polyphenol from Seaweed, Decreases Sleep Latency and Increases Non-Rapid Eye Movement Sleep in Mice. *Marine Drugs*, 2018, **16**(5), p.139.

315. Hosseini A, Sobhanifar MA, Forouzanfar F, et al. Hypnotic Effect of Red Cabbage (Brassica oleracea) on Pentobarbital-Induced Sleep in Mice. *Journal of Pharmacy & Bioallied Sciences*, 2018, **10**(1), pp.48-53.

316. Kim HD, Hong KB, Noh DO, et al. Sleep-inducing effect of lettuce (Lactuca sativa) varieties on pentobarbital-induced sleep. *Food Science and Biotechnology*, 2017, **26**(3), pp.807-814.

317. Pifferi F, Rahman A, Languille S, et al. Effects of dietary resveratrol on the sleep-wake cycle in the non-human primate gray mouse lemur (Microcebus murinus). *Chronobiology International*, 2012, **29**(3), pp.261-70.

318. San AM, Thongpraditchote S, Sithisarn P, et al. Total Phenolics and Total Flavonoids Contents and Hypnotic Effect in Mice of Ziziphus mauritiana Lam. Seed Extract. *Evidence-Based Complementary and Alternative Medicine*, 2013, **2013**, p.835854.

319. Shinozaki A, Misawa K, Ikeda Y, et al. Potent Effects of Flavonoid Nobiletin on Amplitude, Period, and Phase of the Circadian Clock Rhythm in PER2::LUCIFERASE Mouse Embryonic Fibroblasts. *PloS One*, 2017, **12**(2), p.e0170904.

320. Qi G, Mi Y, Fan R, et al. Tea polyphenols ameliorates neural redox imbalance and mitochondrial dysfunction via mechanisms linking the key circadian regular Bmal1. *Food and Chemical Toxicology*, 2017, **110**, pp.189-199.

321. Gadacha W, Ben-Attia M, Bonnefont-Rousselot D, et al. Resveratrol opposite effects on rat tissue lipoperoxidation: pro-oxidant during day-time and antioxidant at night. *Redox Report:communications in free radical research*, 2009, **14**(4), pp.154-8.

322. Colwell CS. Rhythmic coupling among cells in the suprachiasmatic nucleus. *Journal of Neurobiology*, 2000, **43**(4), pp.379–388.

323. Ramis MR, Esteban S, Miralles A, et al. Caloric restriction, resveratrol and melatonin: Role of SIRT1 and implications for aging and related-diseases. *Mechanisms of Ageing and Development*, 2015, **146-148**, pp.28-41.

324. Orozco-Solis R, Ramadori G, Coppari R, et al. SIRT1 relays nutritional inputs to the circadian clock through the sf1 neurons of the ventromedial hypothalamus. *Endocrinology*, 2015, **156**(6), pp.2174–2184.

325. Lagouge M, Argmann C, Gerhart-Hines Z, et al. Resveratrol improves mitochondrial function and protects against metabolic disease by activating SIRT1 and PGC-1alpha. *Cell*, 2006, **127**(6), pp.1109-22.

326. Asher G, Gatfield D, Stratmann M, et al. SIRT1 regulates circadian clock gene expression through PER2 deacetylation. *Cell*, 2008, **134**(2), pp.317–328.

327. Meng X, Li Y, Li S, et al. Dietary Sources and Bioactivities of Melatonin. *Nutrients*, 2017, **9**(4).

328. St-Onge MP, Crawford A and Aggarwal B. Plant-based diets: Reducing cardiovascular risk by improving sleep quality? *Current Sleep Medicine Reports*, 2018, **4**(1), pp.74-78.

329. Herrlinger KA, Nieman KM, Sanoshy KD, et al. Spearmint Extract Improves Working Memory in Men and Women with Age-Associated Memory Impairment. *Journal of Alternative and Complementary Medicine*, 2018, **24**(1), pp.37-47.

330. Manach C, Williamson G, Morand C, et al. Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies. *The American Journal of Clinical Nutrition*, 2005, **81**(1 Suppl), pp.230S-242S.

331. Kuratsune H, Umigai N, Takeno R, et al. Effect of crocetin from Gardenia jasminoides Ellis on sleep: a pilot study. *Phytomedicine*, 2010, **17**(11), pp.840-3.

332. Wightman EL, Haskell-Ramsay CF, Reay JL, et al. The effects of chronic trans-resveratrol supplementation on aspects of cognitive function, mood, sleep, health and cerebral blood flow in healthy, young humans. *British Journal of Nutrition*, 2015, **114**(9), pp.1427-37.

333. Park I, Ochiai R, Ogata H, et al. Effects of subacute ingestion of chlorogenic acids on sleep architecture and energy metabolism through activity of the autonomic nervous

system: a randomised, placebo-controlled, double-blinded cross-over trial. *British Journal of Nutrition*, 2017, **117**(7), pp.979-984.

334. Um MY, Kim JY, Han JK, et al. Phlorotannin supplement decreases wake after sleep onset in adults with self-reported sleep disturbance: A randomized, controlled, double-blind clinical and polysomnographic study. *Phytotherapy Research*, 2018, **32**(4), pp.698-704.

335. Romain C, Alcaraz PE, Chung LH, et al. Regular consumption of HolisFiit, a polyphenol-rich extract-based food supplement, improves mind and body well-being of overweight and slightly obese volunteers: a randomized, double-blind, parallel trial. *International Journal of Food Sciences and Nutrition*, 2017, **68**(7), pp.840-848.

336. Uddin M, Biswas D, Ghosh A, et al. Consumption of Fruitflow® lowers blood pressure in pre-hypertensive males: a randomised, placebo controlled, double blind, cross-over study. *International Journal of Food Sciences and Nutrition*, 2018, **69**(4), pp.494-502.

337. Grassi D, Socci V, Tempesta D, et al. Flavanol-rich chocolate acutely improves arterial function and working memory performance counteracting the effects of sleep deprivation in healthy individuals. *Journal of Hypertension*, 2016, **34**(7), pp.1298-308.

338. Bigelman KA, Chapman DP, Freese EC, et al. Effects of 6 Weeks of Quercetin Supplementation on Energy, Fatigue, and Sleep in ROTC Cadets. *Military Medicine*, 2011, **176**(5), pp.565-572.

339. Cui Y, Niu K, Huang C, et al. Relationship between daily isoflavone intake and sleep in Japanese adults: a cross-sectional study. *Nutrition Journal*, 2015, **14**, p.127.

340. Cao Y, Taylor AW, Zhen S, et al. Soy Isoflavone Intake and Sleep Parameters over 5 Years among Chinese Adults: Longitudinal Analysis from the Jiangsu Nutrition Study. *Journal of the Academy of Nutrition and Dietetics*, 2017, **117**(4), pp.536-544 e2.

Chapter 2: Later chronotype is associated with lower consumption of fruit: cross-sectional associations in UK adults

Manuscript in preparation

I conducted the plasma vitamin C analyses for this chapter which also contributed to the validation of an online 24- hour recall tool published in BMC Medicine:

Wark PA, Hardie LJ, Frost GS, Alwan NA, Carter M, Elliott P, Ford HE, Hancock N, Morris MA, Mulla UZ, **Noorwali EA**, Petropoulou K, Murphy D, Potter GDM, Greenwood DC and Cade JE. Validity of an online 24-hour recall tool (myfood24) for dietary assessment in population studies: comparison with biomarkers and standard interviews. *BMC Medicine*. 2018, **16** (1), pp.136.

2.1 Abstract

Background: Sleep disruption and insufficient intakes of FV are both associated with an increased risk of morbidity and mortality from non-communicable diseases however, evidence of associations between objective sleep measures, chronotype and FV intakes among UK adults is lacking.

Objective: We investigated the cross-sectional associations between objective sleep measures, chronotype and FV intakes and FV biomarkers in healthy UK adults.

Methods: Sleep (onset, offset, duration and mid-sleep time) were measured by SenseWear® armbands in 176 healthy UK adults. FV intakes (servings/day) were assessed using the Oxford WebQ online 24h dietary questionnaire and grouped based on the NDNS categories. Plasma concentrations of total vitamin C and β-carotene were used as biomarkers of FV intakes. Linear regression analyses, adjusting for confounders, were used to assess the cross-sectional associations between sleep measures, chronotype and FV intakes and their associated biomarkers.

Results: In adjusted models, chronotype was negatively associated with FV intakes. Every hour later mid-sleep time was associated with 16% (exp (b) = 0.84, 99% CI 0.71 to 0.99, p=0.008) lower intakes of total fruit. Sleep duration and sleep timing were not associated with FV intakes.

Conclusions: This is the first study to assess the cross-sectional associations between objective sleep measures, chronotype and FV intakes in UK adults. Later chronotype was associated with lower intakes of total fruit. This study adds to the notion that later chronotype is associated with less healthy dietary choices.

Key words: Sleep, fruits and vegetables, nutritional epidemiology

2.2 Introduction

The global rise of non-communicable diseases and premature deaths are troubling. A range of lifestyle and behavioural factors may contribute. Evidence suggests that sleep disruption and low consumption of FV are probable attributable factors (1-3).

In 2013, an estimated 5.6 million premature deaths worldwide may be attributable to FV intakes below 500 grams per day and 7.8 million premature deaths to FV intakes below 800 grams per day (3). In 2017, an estimated 3.9 million deaths worldwide were attributable to inadequate FV consumption according to WHO (4). Increased consumption of FV has been shown to protect against type 2 diabetes (5), coronary heart disease (6), stroke (7) and some cancers (8). A dose-response meta-analysis of prospective studies showed that the consumption of 800 grams per day (10 portions per day) of FV are associated with lower risks of cardiovascular disease, cancer and all-cause mortality (3). Despite these studies, FV consumption remain below the recommended levels (5 portions per day) in the UK (9, 10). Consequently, identifying lifestyle factors, which may influence FV intakes, is a public health priority.

Two previous observational studies have assessed the associations between sleep measures and FV consumption in adults (11, 12). In US pregnant women, total FV consumption was not associated with subjective sleep duration whereas orange and green vegetable consumption were inversely associated with sleep duration (11). Main limitations of this study is the lack of use of objective measures of sleep and a validated dietary assessment tool. A further limitation is FV were grouped to “green vegetables”, “orange vegetables” and “other vegetables” which are not based on genus or total carotenoid content. Another study with subjective report of sleep duration, quality and FV consumption conducted in older Chinese adults (≥65 years) found that participants consuming FV occasionally had lower odds of reporting good quality of sleep compared with daily consumers (12). In addition, less frequent FV consumption was associated with short sleep and long sleep compared to the reference group

Studies that used objective measures of sleep including actigraphy in relation to FV consumption in adults included a small sample size (n=52) found that later sleep timing was associated with fewer servings of FV (13). Another study was conducted in a Hispanic/Latino population reported a positive association between sleep efficiency (the percentage of the sleep period spent asleep) and diet quality. Interestingly, whole fruit intake was the component that contributed the most to the relationship between sleep efficiency and diet quality (14). However, there is a lack of studies assessing the

association between sleep and FV consumption using validated objective methods in UK adults.

Chronotype and its relation to health is increasingly a topic of public health concern. Chronotype has been defined as "*An individual's phase angle of entrainment (for example, the timing of core body temperature nadir relative to dawn*)" (15) which is the preference in timing of activity and sleep referred to as morning or evening type (16). Later chronotype (evening type) was associated with higher risks of some diseases such as cardiovascular disease (17) type 2 diabetes (18) metabolic disorders (19) bipolar disorder (20) and obesity (21). In a recent study conducted using the UK Biobank, a large prospective population based cohort study including 433,268 adults, later chronotype was associated with higher odds of psychological disorders, diabetes, neurological disorders, gastrointestinal disorders and respiratory disorders. Additionally, later chronotype was associated with an increased risk of all-cause mortality compared to earlier chronotype (22).

These findings are worrisome for public health, and thus studies assessing the associations between chronotype and other lifestyle behaviours such as FV consumption are necessary (23). A main limitation of the previous studies is the lack of usage of objective methods to measure chronotype such as actimetry. There is a necessity to assess the associations between chronotype and FV consumption using validated objective methods.

The associations between sleep measures, chronotype and FV consumption are not well characterized in adults (24). Therefore, we assessed the cross-sectional associations between objective sleep measures, chronotype, FV consumption and biomarkers of FV in UK adults.

2.3 Methods

The data analysed in this chapter are from a study designed to assess the validity of the online dietary recall tool myfood24 which is described elsewhere (25). In this study I used data from the validation study for a different purpose.

2.3.1 Participants

Participants were recruited using a list of London-based addresses obtained from the post office and advertising posters in the National Institute of Health Research /Wellcome Trust Clinical Research Facility at Hammersmith hospital (Imperial College Healthcare NHS Trust, London, UK). In addition, the Clinical research Facility contact list was used

for participants' recruitment. A group of primary care professionals and practices that previously showed interest in participating in research projects called the North-West London Primary Care Research Network were also contacted. Participants represented the UK adult population aged 18-68 years, English speakers, non-pregnant, weight-stable and had access for internet and telephone. The study was approved by the West London Research Ethics Committee (number 14/SC/1267) and was conducted in accordance with the Declaration of Helsinki. Participants provided written informed consent and received a £100 reward on completion of the study.

2.3.2 Study Design

The study design outline is shown in Figure 2.1. Respondents were invited to attend a screening visit to confirm eligibility, receive a detailed explanation of the study protocol, provide informed consent and if eligible they completed a health screening at the Clinical Research Facility. During the health screening visit, blood pressure was measured using a digital monitor (Omron, Kyoto, Japan) after participants rested supine for ~30 minutes, weight using scales (Tanita Corporation, Tokyo, Japan) and height using a stadiometer (Seca, Hamburg, Germany) and cardiac function was assessed by electrocardiography. Blood samples (22 ml) were taken for full blood count, urea and electrolytes, liver function tests and lipid profile. Participants were asked to complete a general health and lifestyle questionnaire, the SCOFF questionnaire in order to assess the possible presence of an eating disorder and a technology readiness questionnaire. After the screening visit, participants visited the Clinical Research Facility up to 3 times, separated by ≥ 2 weeks. Study visits took place between 12/06/2014 and 07/08/2015. Before each visit, participants were instructed not to eat for ≥ 4 hours and to wear a SenseWear® armband (Body Media Inc., Pittsburgh, Pennsylvania, USA) for ~ 24 hours to estimate sleep and physical activity. After 1-5 days of each visit, participants completed an online 24-hour dietary recall named the Oxford WebQ online assessment tool which is being used by the UK Biobank project (26).

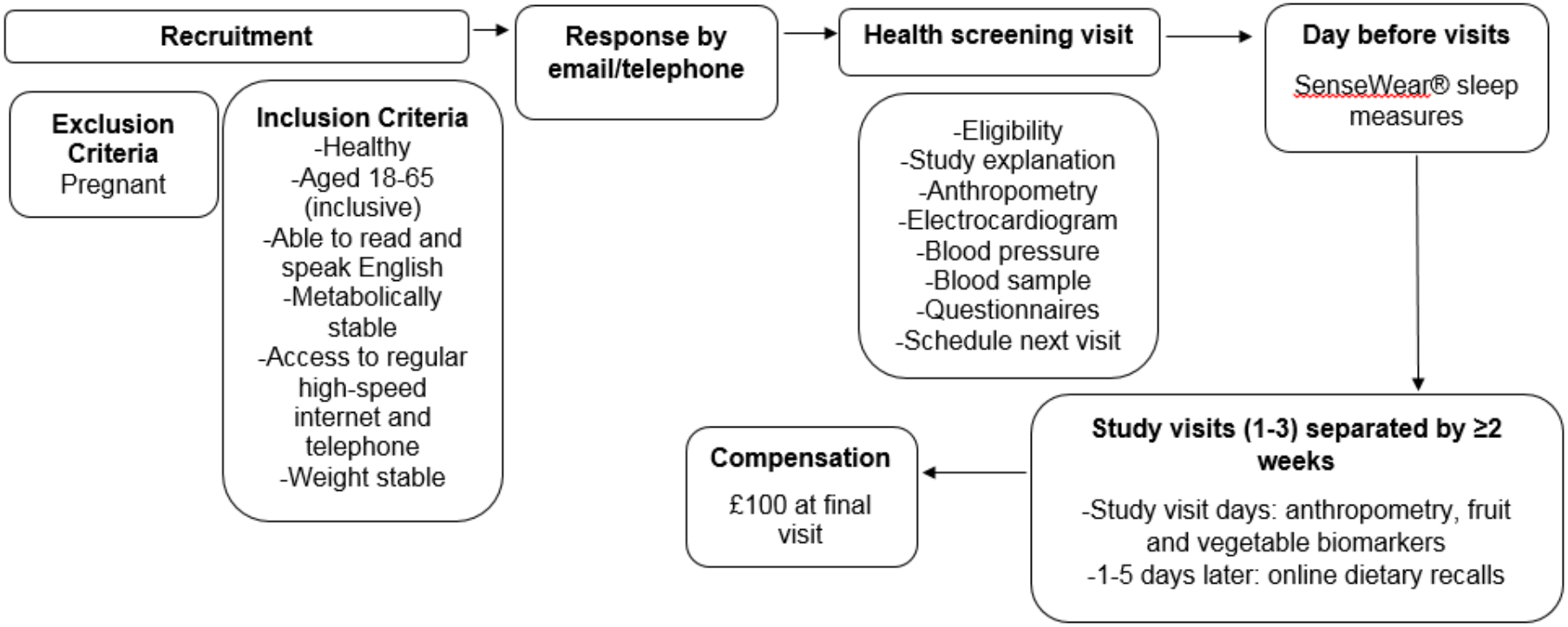

Figure 2.1. Study design overview.

2.3.3 Sleep measures and chronotype

Participants were instructed to wear a SenseWear® armband the day before each visit for 24h to estimate sleep and physical activity. It was wore on the midline of the left triceps brachii and participants were instructed to only remove them when bathing. The accelerometers did not give participants information regarding activity and sleep to avoid feedback effects. In several populations, sleep estimates from SenseWear® armband have shown good agreement with polysomnographic sleep measures (27-29).

Sleep scoring of sleep records was completed by another researcher, Gregory Potter, and only included nocturnal weekdays because apart from one participant all sleep records were during weekday nights. What appeared to be daytime naps were not scored. Sleep onset was defined as the first minute of registered sleep in a 20-minute period in which there were ≥ 19 minutes of sleep recorded, this was conducted because it has been shown that this improves agreement between actimetric estimates of sleep and polysomnographic measures (30). Sleep offset was defined as the first minute of registered wakefulness in a 20-minute period in which there were ≥ 19 minutes of wakefulness or activity recorded. Sleep period was calculated as sleep offset minus sleep onset (see Appendix B (B.1.) for an example of how sleep variables were defined from the raw activity data). Currently, the best marker of circadian phase is the time point at which melatonin rises before sleep (dim-light melatonin onset (DLMO)) and a strong correlation was shown previously between DLMO and mid-sleep time on workdays (r=0.71, $p<0.001$) therefore, mid-sleep time was calculated as the halfway time in sleep period and was used as a proxy of chronotype given its strong correlation with DLMO (31). Actimetry data does not include cut-offs indicating early or late chronotypes such as in the MEQ that directly asks whether you are a “definitely a morning type”, “rather more a morning type than evening type”, rather more an evening type than a morning type” and definitely an evening type. However, the MEQ is clearly limited by its lack of quantitative estimates of actual sleep timing. Since participants did not provide subjective assessment of their chronotype (morning or evening type), in this study, every hour later of mid-sleep time is considered as later chronotype and not “evening chronotypes”. Sleep duration was calculated as the sum of sleeping minutes recorded during the sleep period. In this study, I used the mean values of sleep measures for our analyses if participants had multiple nights of sleep recorded.

2.3.4 FV intakes

Oxford WebQ online assessment tool

The Oxford WebQ is an online dietary questionnaire that obtains information on the quantities of all foods and drinks consumed over the previous day. The development of Oxford WebQ has been described and relative validity assessed with an interviewer based 24 h dietary recall elsewhere (32). For the analyses of this study, we used FV intakes recorded for the previous day (servings/day) and the average of servings were used for participants with more than one diet recall. FV items were grouped according to the NDNS categories which is based on genus and total carotenoid content (33) and are shown in detail in (Appendix B (B.2.)).

2.3.5 FV Biomarkers

During participant visits to the Clinical Research Facility, 40 ml of blood samples were collected into lithium heparin tubes. Samples were then centrifuged at 200xg for 10 minutes and plasma was collected and frozen at -80 ºC. For this study, plasma concentrations of total vitamin C (dehydroascorbic and ascorbic acid) and β-carotene were measured as they are correlated with FV consumption (34, 35). I conducted the plasma vitamin C analyses that contributed to the validation of an online 24-hour recall tool (myfood24) (25) using high performance liquid chromatography (HPLC) as previously described (36) in the Molecular Epidemiology Unit at the University of Leeds with detection at 270nm for ascorbic acid (Appendix B (B.3.)). β-carotene was analysed by another researcher, David Murphy, using HPLC with 452nm detection.

2.3.6 Statistical analyses

Linear regression analyses were used to determine the associations between sleep measures, chronotype, and FV intakes and biomarkers. All participants were included in the main analyses and a directed acyclic graph was used to select variables for adjustment (Appendix B (B.4.)). We adjusted for age, sex, socioeconomic status (SES) based on the Office of National Statistics-Socio-Economic Classification (NS-SEC) (37), ethnicity (white, non-white), smoking (smoker, non-smoker) and total energy intake. The final number (n column in Table 2.2) of participants included in the analyses indicates complete data of all covariates included in the model, and difference in (n) is due to missing data of any of the included covariates in the model.

For regression analyses, I used histogram plots to check normal distribution. Positively skewed outcomes including FV consumption and biomarkers were log-transformed and back transformed. The values in Table 2.2. correspond to changes in ratio of the original outcome variable. P values of ≤0.01 represent statistical significance and statistical analyses were conducted using IC Stata version 15.1 statistical software (38).

2.4 Results

Two hundred and eighty-nine respondents were invited to the first health screening visit. Two hundred and forty of them attended and passed the health screen. Before beginning the study, 27 participants withdrew and 18 participants had unavailable sleep data. 212 participants provided samples for biomarker analyses on at least one occasion, 164 participants completed the online Oxford WebQ on at least one occasion. Participant characteristics are summarised in Table 2.1.

Table 2.1. Participant characteristics stratified by sex.

Characteristic	Women (n= 127)	Men (n= 89)
	Mean (95% CI)	**Mean (95% CI)**
Age (Years)	43(41, 46)	44 (40, 47)
Body mass index (kg/m^2)	25 (24, 25)	26 (25, 27)
Physical activity duration (minutes/day)	103 (89,117)	152 (128,176)
Weekday sleep		
Sleep onset time	23:59 (23:50, 00:21)	00:30 (00:10, 00:60)
Sleep offset time	7:24 (7:05, 7:43)	7:25 (7:20,7:50)
Mid-sleep time	3:40 (3:30, 3:50)	3:50 (3:30, 4:00)
Sleep duration (hours)	6.3 (6.1,6.5)	5.8 (5.6,6.1)
Total FV intakes (servings/day)	4.6 (3.9, 5.2)	4.2 (3.6, 4.9)
Plasma vitamin C (μM)	71 (68,75)	57 (52,61)
Plasma β-carotene (μM)	0.8 (0.7,0.9)	0.5 (0.4,0.7)
	% (95% CI)	**% (95% CI)**
Ethnicity (White)	74 (65, 80)	76 (66, 83)
Longstanding illness (Yes)	9 (5, 15)	10 (5, 18)
SES (Lower managerial/professional & higher supervisory occupations)	36 (28, 44)	28 (20, 38)
Current smoker	9 (5, 15)	9 (4, 17)
Vegetarian/vegan (Yes)	7 (3, 13)	7 (3, 15)
Currently drink alcohol	80 (73, 86)	84 (75, 90)
Marital status (single/never married)	58 (49, 66)	55 (44, 65)

Legend: FV (fruits and vegetables), SES (socio-economic status).

A scatter plot to assess the correlation between vitamin C nutrient intake measured by Oxford WebQ and plasma vitamin C showed that no linear association was evident between them (Figure 2.2.). Pearson correlation coefficient r=0.1 (95% CI -0.08 to 0.2, p = 0.08) for 162 observations. A scatter plot to assess the correlation between carotene nutrient intake measured by Oxford WebQ and plasma β-carotene showed a positive linear association between them (Figure 2.3.). Pearson correlation coefficient r= 0.4 (95% CI 0.2 to 0.5, p <0.01) for 123 observations

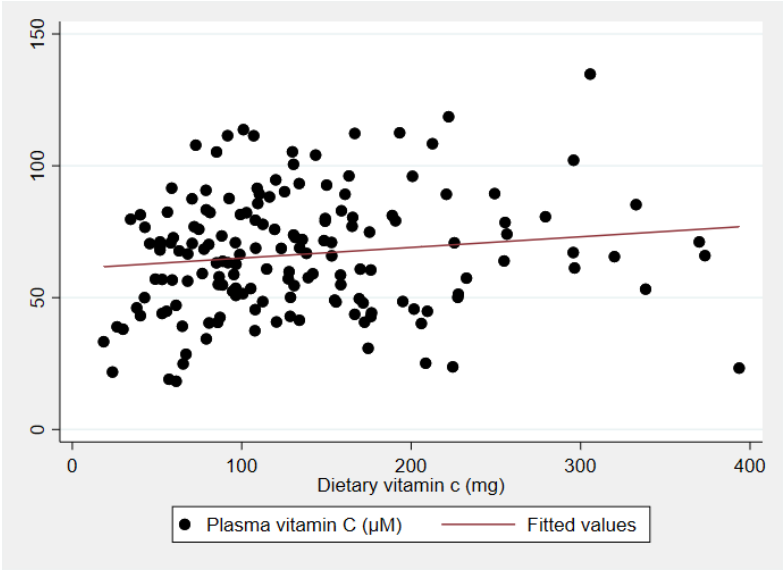

Figure 2.2. Scatter plot assessing the correlation between plasma vitamin C and dietary vitamin C.

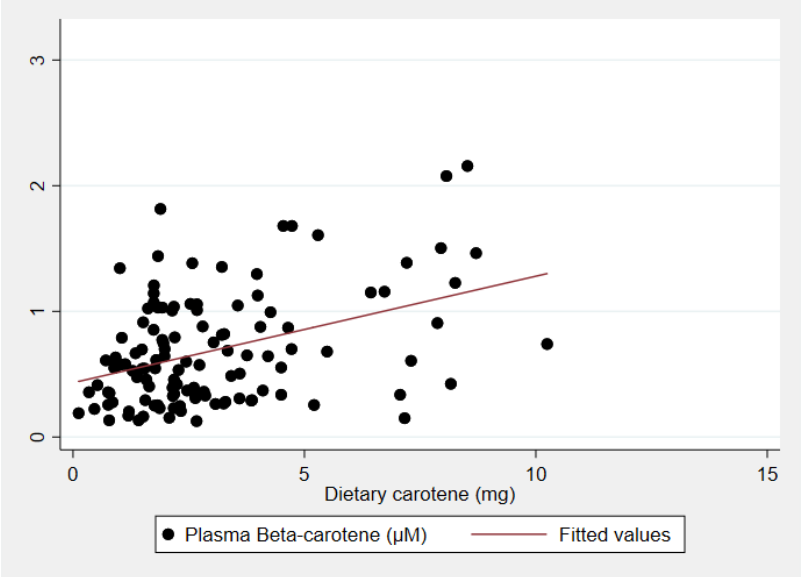

Figure 2.3. Scatter plot assessing the correlation between plasma β-carotene and dietary carotene.

2.4.1 The cross-sectional associations between objective sleep, chronotype and FV consumption

In adjusted models (Table 2.2.), mid-sleep time (chronotype) was negatively associated with total fruit intake. Every hour later, mid-sleep time was associated with 16% (exp (b) = 0.84, 99% CI 0.71 to 0.99, p=0.008) lower intakes of total fruit. Sleep onset and sleep offset also showed borderline significant negative association with total fruit intakes. Every hour later sleep onset was associated with 13% (exp (b) = 0.87, 99% CI 0.76, 1.02, p=0.01) lower intakes of total fruit and every hour later sleep offset was associated with 13% (exp (b) = 0.87, 99% CI 0.74 to 1.03, p= 0.03) lower intakes of total fruit.

Sleep onset and mid-sleep time showed borderline negative associations with plasma vitamin C. Every hour later sleep onset was associated with 5% lower levels of plasma vitamin C (exp (b) = 0.95, 99% CI 0.91 to 1.009, p=0.03) and every hour later mid-sleep time was associated with 5% lower levels of plasma vitamin C (exp (b) = 0.95, 99% CI 0.89 to 1.01, p=0.06). Sleep duration was not associated with FV consumption or vitamin C and β-carotene biomarkers

Table 2.2. The cross-sectional associations between objective sleep, chronotype and FV consumption

Sleep duration (hours/d)						
Models	**Unadjusted**			**Adjusted***		
FV (servings/day)	**Changes in ratio per additional hour (99% CI)**	**P value**	**n**	**Changes in ratio per additional hour (99% CI)**	**P value**	**n**
Total Fruit	1.05 (0.90,1.23)	0.3	126	1.05 (0.90,1.23)	0.3	123
Fruit juice	0.95 (0.81,1.10)	0.3	86	0.92 (0.78,1.09)	0.2	82
Dried fruit	0.92 (0.76,1.11)	0.2	42	1.01 (0.81,1.27)	0.8	42
Salad	1.01 (0.80,1.27)	0.8	69	1.06 (0.81,1.40)	0.5	67
Tomato	0.95 (0.76,1.17)	0.5	92	0.97 (0.76,1.23)	0.7	89
Brassicaceae	1.05 (0.84,1.30)	0.5	63	0.95 (0.73,1.25)	0.6	60
Yellow, red, green veg	1.04 (0.85,1.27)	0.5	89	1.06 (0.86,1.31)	0.3	87
Other veg	0.97 (0.83,1.13)	0.6	133	1.01 (0.87,1.17)	0.7	128
Total veg	0.99 (0.85,1.16)	0.9	138	0.99 (0.85,1.15)	0.8	133
Total FV	1.03 (0.89,1.19)	0.5	140	1.05 (0.92,1.20)	0.2	135
FV biomarkers						
Vitamin C (μM)	1.04 (0.99,1.10)	0.1	182	1.02 (0.96,1.08)	0.2	134
β-carotene (μM)	1.03 (0.92,1.17)	0.4	133	1.04 (0.91,1.19)	0.3	100
Sleep onset (24 hour clock)						
	Unadjusted			**Adjusted***		

FV (servings/day)	Changes in ratio per additional hour (99% CI)	P value	n	Changes in ratio per additional hour (99% CI)	P value	n
Total fruit	0.88 (0.77,1.009)	0.02	126	0.87 (0.76,1.02)	0.01	123
Fruit juice	1.03 (0.90,1.17)	0.4	86	1.01 (0.88,1.16)	0.7	82
Dried fruit	0.99 (0.82,1.21)	0.9	42	0.94 (0.77,1.14)	0.4	42
Salad	1.01 (0.81,1.27)	0.8	69	1.05 (0.80,1.36)	0.6	67
Tomato	0.97 (0.81,1.17)	0.7	92	0.98 (0.80,1.19)	0.8	89
Brassicaceae	0.98 (0.80,1.20)	0.8	63	1.03 (0.81,1.30)	0.7	60
Yellow, red, green veg	0.97 (0.82,1.15)	0.7	89	0.97 (0.82,1.16)	0.7	87
Other veg	1.09 (0.96, 1.25)	0.06	133	1.10 (1.97,1.24)	0.04	128
Total veg	1.05 (0.91,1.20)	0.3	138	1.06 (0.94,1.21)	0.1	133
Total FV	0.97 (0.85,1.10)	0.6	140	0.97 (0.87,1.09)	0.6	135
FV biomarkers						
Vitamin C (µM)	0.96 (0.91,1.008)	0.03	182	0.95 (0.91,1.009)	0.03	134
β-carotene (µM)	0.91 (0.83,1.01)	0.03	133	0.96 (0.86,1.07)	0.3	100
Sleep offset (24 hour clock)						
	Unadjusted			**Adjusted***		
FV (servings/day)	**Changes in ratio per additional hour (99% CI)**	**P value**	**n**	**Changes in ratio per additional hour (99% CI)**	**P value**	**n**
Total fruit	0.91 (0.78,1.07)	0.1	126	0.87 (0.74,1.03)	0.03	123
Fruit juice	1.06 (0.91,1.24)	0.2	86	1.02 (0.85,1.21)	0.7	82
Dried fruit	0.94 (0.72,1.23)	0.6	42	0.93 (0.71,1.22)	0.4	42
Salad	0.97 (0.75,1.26)	0.8	69	1.01 (0.74,1.38)	0.8	67
Tomato	0.86 (0.70,1.06)	0.07	92	0.91 (0.72,1.15)	0.3	89
Brassicaceae	0.95 (0.75,1.21)	0.6	63	0.91 (0.69,1.21)	0.4	60
Yellow, red, green veg	1.01 (0.81,1.25)	0.8	89	1.04 (0.82,1.33)	0.5	87
Other veg	1.06 (0.91,1.24)	0.2	133	1.12 (0.96,1.31)	0.05	128
Total veg	1.06 (0.90,1.24)	0.3	138	1.06 (0.90,1.24)	0.3	133
Total FV	0.98 (0.84,1.14)	0.7	140	0.98 (0.85,1.13)	0.8	135
FV biomarkers						
Vitamin C (µM)	0.98 (0.93,1.04)	0.6	182	0.97 (0.91,1.03)	0.2	134
β-carotene (µM)	0.92 (0.81,1.04)	0.09	133	0.96 (0.83,1.11)	0.5	100
Mid-sleep (24 hour clock)						
	Unadjusted			**Adjusted***		
FV (servings/day)	**Changes in ratio per additional hour (99% CI)**	**P value**	**n**	**Changes in ratio per additional hour (99% CI)**	**P value**	**n**
Total fruit	0.87 (0.78,1.004)	0.05	126	0.84 (0.71, 0.99)	0.008	123
Fruit juice	1.05 (0.90,1.23)	0.3	86	1.02 (0.86,1.21)	0.7	82
Dried fruit	0.97 (0.74,1.26)	0.7	42	0.92 (0.71,1.19)	0.4	42

Salad	1.001 (0.75,1.32)	0.9	69	1.04 (0.75,1.45)	0.6	67
Tomato	0.91 (0.73,1.13)	0.2	92	0.94 (0.74,1.19)	0.5	89
Brassicaceae	0.96 (0.75,1.23)	0.7	63	0.98 (0.73,1.30)	0.8	60
Yellow, red, green veg	0.98 (0.79,1.22)	0.8	89	1.004 (0.79,1.26)	0.9	87
Other veg	1.11 (0.94,1.30)	0.08	133	1.14 (0.97,1.33)	0.02	128
Total veg	1.07 (0.90,1.26)	0.2	138	1.08 (0.92,1.26)	0.1	133
Total FV	0.97 (0.83,1.13)	0.6	140	0.97 (0.84,1.12)	0.6	135
FV biomarkers						
Vitamin C (μM)	0.96 (0.91,1.02)	0.1	182	0.95 (0.89,1.01)	0.06	134
β-carotene (μM)	0.90 (0.79,1.02)	0.03	133	0.95 (0.83,1.09)	0.4	100

Legend: FV (fruits and vegetables), veg (vegetables).
*Adjusted for age, sex, socio-economic status, ethnicity, smoking and total energy intake

2.5 Discussion

To our knowledge, this is the first study to report on cross-sectional associations between objective sleep measures, chronotype and FV consumption using a validated method, and their associated biomarkers in UK adults. In addition, no other study grouped FV items based on their genus and carotene content. Our results showed that plasma vitamin C was not correlated with dietary vitamin C whereas dietary carotene was positively correlated with plasma β-carotene. In adjusted models, mid-sleep time used as a proxy of chronotype was negatively associated with total fruit consumption. Every hour later mid-sleep time was associated with 16% lower intakes of total fruit. Collectively, these findings suggest that among healthy UK adults, later mid-sleep time (chronotype) was associated with lower intakes of total fruit.

Biomarkers of vitamin C and β-carotene were used as a surrogate marker of FV consumption and are classified as concentration biomarkers (39). In this study, plasma vitamin C was not correlated with dietary vitamin C whereas plasma β-carotene was positively associated with dietary carotene. These inconsistent results may be that concentration biomarkers are based on the biomarker concentration in the specimen and have high-inter individual variability because they do not have a consistent relationship between intake and excretion. Another factor to consider is that vitamin C is a water-soluble vitamin and renal excretion is minimised for lower plasma vitamin C affecting biomarker concentration. Furthermore, the relationship between vitamin C intake and absorption is linear for vitamin C only for intakes below ~100 mg/day and intakes above 120 mg/day reach a plateau (40). Another plausible reason of why we didn't find correlation between dietary vitamin C and plasma vitamin C is that the strength of correlation may be influenced by the sample size (41).

Our results showed that sleep onset and mid-sleep time showed borderline negative associations with plasma vitamin C however, sleep duration was not associated with FV consumption or vitamin C and β-carotene biomarkers. These results are in contrast with another study using sleep as the outcome and biomarkers as the exposures. They reported that α-carotene biomarker was inversely associated with sleepiness and a positive association was found between β-carotene and sleepiness. Furthermore, serum total carotenoid concentrations were associated with an increased risk of short sleep (5-6 hours/day) compared to normal sleep duration (7-8 hours/day) (42). The distinctive results may be due to the different sample sizes, our study had a small sample size compared to Beydoun et al that included ~3000 adults. Another factor is the different populations, Beydoun et al included US adults whereas we included UK adults. Additionally, sleep assessment was self-reported using a computer assisted interview in their study which may cause over-reporting (43) whereas we used objective actimetry data .Sleep measures were categorized in their study in contrast to our study that used continuous variables due to the small sample size. More studies are needed to clarify the associations between nutritional biomarkers and sleep among UK adults.

Our results on later chronotype associated with lower intakes of total fruit are supported with the findings of other cross-sectional studies in adolescents (44, 45) despite the usage of different methods to measure chronotype. Arora and Taheri (44) measured chronotype by asking one question from the MEQ (46) whereas Malone and colleagues used both the MEQ and mid-point of sleep. Furthermore, later chronotype assessed by MEQ was associated with lower intakes of fruit and green, yellow and white vegetables in Japanese nurses (47). Similarly, Finnish adults with later chronotype consumed less fruit (48). Other studies only found an association between later chronotype and lower intakes of vegetables (49-51). Whereas similar to our study, no association was found between chronotype, vegetable and salad intakes in German adolescents (52) and among Brazilian undergraduate students (53). Two cross-sectional studies conducted in UK adults from the UK Biobank project showed that early chronotypes consumed more servings of FV compared to later chronotypes (54) and later chronotype was associated with higher odds of consuming <5 servings/day of FV compared with earlier chronotypes.

The previous studies showed that later chronotypes tend to have lower intakes of FV. However, the results are contradictory and a main limitation of the previous studies is the lack of usage of objective methods to measure chronotype. The reason for this discrepancy between studies is unclear. We measured chronotype using actimetry

whereas all of the other studies used subjective measures. In addition, several studies were conducted in adolescents (44, 45, 52) which are difficult to compare with adults due to their delay in circadian rhythms that occur in association with puberty and external factors such as early school start times (55). Another plausible explanation for the different results is the categorisation of FV in this study based on genus and total carotenoid content which was not used in any of the previous studies. Furthermore, the use of different statistical methods and covariate adjustment may be another explanation. We used a directed acyclic graph to address confounding for making valid causal inferences (56) whereas the previous studies did not use this method.

The previous studies also found that later chronotype has been associated with less healthy behaviours such as smoking (54), physically inactive with sedentary behaviour (21) consuming more alcohol and caffeine (from coffee and cola) compared to early chronotypes (57). This may be a justification of the low consumption of FV in late chronotypes. Plausible mechanisms underlying the association between chronotype and FV consumption may include homeostatic (metabolic) and non-homeostatic (psychological features) (48). Disturbances in chronotype may result partly or independently from short sleep duration. Short sleep duration may result in changes of satiety hormones leptin and ghrelin which leads to an increase in high energy foods and potentially to lower consumption of FV. Non-homeostatic mechanisms relating chronotype with FV consumption may be through physical activity. Late chronotypes tend to stay awake late and have irregular schedules with more sedentary activities at night such as watching TV or the use of electronic devices. These sedentary activities are usually accompanied with unhealthy snacking that require minimum preparation. This potentially may lead to lower consumption of FV in late chronotypes due to the requirement of preparation of FV such as cutting, peeling and cooking.

In contrast to some prior research (11, 13), we did not find an association between sleep duration and timing with FV consumption. This inconsistency may be due to the different populations and methods used. Alternatively, our study may have been underpowered to detect subtle associations. Duke and colleagues explored the associations between FV consumption as exposures and sleep duration (11) in pregnant women whereas, pregnant women were excluded from our study. Another possible reason may be that we measured sleep duration using SenseWear® armbands that has previously shown agreement with polysomnographic sleep measures (27-29) and are well suited to use in studies of free-living participants whereas sleep duration was self-reported by Duke et

al. Additionally, we used the validated Oxford WebQ tool while Duke et al assessed FV consumption by asking questions on frequency regarding the previous month (11).

Later sleep timing was associated with fewer servings of FV consumption in 52 US adults (13). Although we included a larger group of adults we did not find an association between sleep timing and FV consumption. This may be due to the length of wearing the armbands, Baron and colleagues (13) used wrist actigraphy for 7 days while we used the armbands for 1-3 days. Additionally, the armbands are sensitive in detecting sleep but have lower wake detection rates (29). A further plausible explanation is the use of different dietary assessment methods. Experimental studies manipulating sleep timing relative to FV consumption will clarify the contradictory results of the previous studies.

Unlike previous studies, a clear strength of our work is the use of a diet recall tool that has been validated and accurate sleep measurement devices. Nevertheless, we acknowledge that our work has limitations. Sleep measures included only weekdays and few nights of sleep were measured for each participant. In addition, our study included a small sample size.

In conclusion, later chronotype was associated lower intakes of total fruit but, sleep duration and timing were not associated with FV consumption. Our findings strengthens the notion that later chronotype is associated with less healthy behaviours. Perhaps chronotype is another piece in the complex puzzle of the increasing trend of morbidity and mortality (23). The cross-sectional nature of the study does not infer causality that later chronotype results in lower consumption of FV. Prospective and experimental studies are needed to clarify the relationships between sleep measures, chronotype and FV consumption.

The following chapters of this thesis will focus on assessing the prospective associations between FV consumption as the exposure and sleep duration as the outcome using a large cohort of UK women (Chapter 3). Additionally, the cross-sectional, potential non-linear associations between sleep duration as the exposure and FV consumption as the outcomes will be explored using a nationally representative sample of UK adults with disaggregated data of FV that helps in estimating the total intakes of FV (Chapter 4). Finally, prospective and potential non-linear associations will be explored between sleep duration (exposure) and FV consumption (outcomes) using a large cohort of UK women (Chapter 5).

References of Chapter 2

1. Jike M, Itani O, Watanabe N, et al. Long sleep duration and health outcomes: A systematic review, meta-analysis and meta-regression. *Sleep Medicine Reviews*, 2018, **39**, pp.25-36.

2. Itani O, Jike M, Watanabe N, et al. Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression. *Sleep Medicine*, 2017, **32**, pp.246-256.

3. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies. *International Journal of Epidemiology*, 2017, **46**(3), pp.1029-1056.

4. WHO. *Increasing fruit and vegetable consumption to reduce the risk of non-communicable diseases* [online]. 2017. [Accessed 5 March 2018]. Available from: https://www.who.int/elena/titles/fruit_vegetables_ncds/en/.

5. Muraki I, Imamura F, Manson JE, et al. Fruit consumption and risk of type 2 diabetes: results from three prospective longitudinal cohort studies. *BMJ*, 2013, **347**, p.f5001.

6. He F, Nowson C, Lucas M, et al. Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies. *Journal of Human Hypertension*, 2007, **21**(9), pp.717-728.

7. Hu D, Huang J, Wang Y, et al. Fruits and vegetables consumption and risk of stroke: a meta-analysis of prospective cohort studies. *Stroke*, 2014, **45**(6), pp.1613-9.

8. World Cancer Research Fund / American Institute for Cancer Research. *Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective.* [online]. 2007. [Accessed 5 April 2017]. Available from: http://discovery.ucl.ac.uk/4841/1/4841.pdf.

9. Bates B, Lennox A, Prentice A et al. *National Diet and Nutrition Survey Results from years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009-2011/2012).* [online]. 2014. [Accessed 6 May 2015]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/594361/NDNS_Y1_to_4_UK_report_full_text_revised_February_2017.pdf.

10. Roberts C, Steer T, Maplethorpe N, et al. *National Diet and Nutrition Survey Results from years 7 and 8 (combined) of the Rolling Programme (2014/2015 to 2015/2016).* [online]. 2018. [Accessed 9 January 2019]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/699241/NDNS_results_years_7_and_8.pdf.

11. Duke CH, Williamson JA, Snook KR, et al. Association Between Fruit and Vegetable Consumption and Sleep Quantity in Pregnant Women. *Maternal and Child Health Journal*, 2017, **21**(5), pp.966-973.

12. Lee YH, Chang YC, Lee YT, et al. Dietary patterns with fresh fruits and vegetables consumption and quality of sleep among older adults in mainland China. *Sleep and Biological Rhythms*, 2018, **16**(3), pp.293-305.

13. Baron KG, Reid KJ, Kern AS, et al. Role of sleep timing in caloric intake and BMI. *Obesity (Silver Spring)*, 2011, **19**(7), pp.1374-81.

14. Mossavar-Rahmani Y, Weng J, Wang R, et al. Actigraphic sleep measures and diet quality in the Hispanic Community Health Study/Study of Latinos Sueno ancillary study. *Journal of Sleep Research*, 2017, **26**(6), pp.739-746.

15. Potter GD, Skene DJ, Arendt J, et al. Circadian Rhythm and Sleep Disruption: Causes, Metabolic Consequences, and Countermeasures. *Endocrine Reviews*, 2016, **37**(6), pp.584-608.

16. Roenneberg T, Wirz-Justice A and Merrow M. Life between clocks: Daily temporal patterns of human chronotypes. *Journal of Biological Rhythms*, 2003, **18**(1), pp.80-90.

17. Reutrakul S and Knutson KL. Consequences of Circadian Disruption on Cardiometabolic Health. *Sleep Medicine Clinics*, 2015, **10**(4), pp.455-68.

18. Merikanto I, Lahti T, Puolijoki H, et al. Associations of chronotype and sleep with cardiovascular diseases and type 2 diabetes. *Chronobiology International*, 2013, **30**(4), pp.470-7.

19. Yu JH, Yun CH, Ahn JH, et al. Evening Chronotype Is Associated With Metabolic Disorders and Body Composition in Middle-Aged Adults. *Journal of Clinical Endocrinology and Metabolism*, 2015, **100**(4), pp.1494-1502.

20. Melo MCA, Abreu RLC, Linhares Neto VB, et al. Chronotype and circadian rhythm in bipolar disorder: A systematic review. *Sleep Medicine Reviews*, 2017, **34**, pp.46-58.

21. Patterson F, Malone SK, Grandner MA, et al. Interactive effects of sleep duration and morning/evening preference on cardiovascular risk factors. *European Journal of Public Health*, 2018, **28**(1), pp.155-161.

22. Knutson KL and Von Schantz M. Associations between chronotype, morbidity and mortality in the UK Biobank cohort. *Chronobiology International*, 2018, **35**(8), pp.1045-1053.

23. Almoosawi S, Vingeliene S, Gachon F, et al. Chronotype: Implications for Epidemiologic Studies on Chrono-Nutrition and Cardiometabolic Health. *Advances in Nutrition*, 2019, **10**(1), pp.30-42.

24. Dashti HS, Scheer FA, Jacques PF, et al. Short sleep duration and dietary intake: epidemiologic evidence, mechanisms, and health implications. *Advances in Nutrition*, 2015, **6**(6), pp.648-59.

25. Wark PA, Hardie LJ, Frost GS, et al. Validity of an online 24-h recall tool (myfood24) for dietary assessment in population studies: comparison with biomarkers and standard interviews. *BMC Medicine*, 2018, **16**(1), p.136.

26. Galante J, Adamska L, Young A, et al. The acceptability of repeat Internet-based hybrid diet assessment of previous 24-h dietary intake: administration of the Oxford WebQ in UK Biobank. *British Journal of Nutrition*, 2016, **115**(4), pp.681-6.

27. Sharif MM and Bahammam AS. Sleep estimation using BodyMedia's SenseWear (TM) armband in patients with obstructive sleep apnea. *Annals of Thoracic Medicine*, 2013, **8**(1), pp.53-57.

28. Roane BM, Van Reen E, Hart CN, et al. Estimating sleep from multisensory armband measurements: validity and reliability in teens. *Journal of Sleep Research*, 2015, **24**(6), pp.714-21.

29. Shin M, Swan P and Chow CM. The validity of Actiwatch2 and SenseWear armband compared against polysomnography at different ambient temperature conditions. *Sleep Science*, 2015, **8**(1), pp.9-15.

30. Cole RJ, Kripke DF, Gruen W, et al. Automatic sleep/wake identification from wrist activity. *Sleep*, 1992, **15**(5), pp.461-9.

31. Kantermann T and Burgess HJ. Average mid-sleep time as a proxy for circadian phase. *Psych Journal*, 2017, **6**(4), pp.290-291.

32. Liu B, Young H, Crowe FL, et al. Development and evaluation of the Oxford WebQ, a low-cost, web-based method for assessment of previous 24 h dietary intakes in large-scale prospective studies. *Public Health Nutrition*, 2011, **14**(11), pp.1998-2005.

33. Fitt E, Mak TN, Stephen AM, et al. Disaggregating composite food codes in the UK National Diet and Nutrition Survey food composition databank. *European Journal of Clinical Nutrition*, 2010, **64 Suppl 3**, pp.S32-6.

34. Al-Delaimy WK, Slimani N, Ferrari P, et al. Plasma carotenoids as biomarkers of intake of fruits and vegetables: ecological-level correlations in the European Prospective Investigation into Cancer and Nutrition (EPIC). *European Journal of Clinical Nutrition*, 2005, **59**(12), pp.1397-1408.

35. Souverein OW, De Vries JHM, Freese R, et al. Prediction of fruit and vegetable intake from biomarkers using individual participant data of diet-controlled intervention studies. *British Journal of Nutrition*, 2015, **113**(9), pp.1396-1409.

36. White KL, Chalmers DM, Martin IG, et al. Dietary antioxidants and DNA damage in patients on long-term acid-suppression therapy: a randomized controlled study. *British Journal of Nutrition*, 2002, **88**(3), pp.265-71.

37. Office for National Statistics. *The National Statistics Socio-economic classification (NS-SEC)* [online]. [Accessed 10 March 2018]. Available from: https://www.ons.gov.uk/methodology/classificationsandstandards/otherclassifications/thenationalstatisticssocioeconomicclassificationnssecrebasedonsoc2010.

38. StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.

39. Lovegrove J, Hodson L, Sharma S, et al. *Nutrition research methodologies.* The Nutrition Society textbook series. Chichester, West Sussex: Wiley Blackwell,, 2015.

40. Jenab M, Slimani N, Bictash M, et al. Biomarkers in nutritional epidemiology: applications, needs and new horizons. *Human Genetics*, 2009, **125**(5-6), pp.507-25.

41. Bates BT, Zhang SN, Dufek JS, et al. The effects of sample size and variability on the correlation coefficient. *Medicine and Science in Sports and Exercise*, 1996, **28**(3), pp.386-391.

42. Beydoun MA, Gamaldo AA, Canas JA, et al. Serum nutritional biomarkers and their associations with sleep among US adults in recent national surveys. *PloS One*, 2014, **9**(8), p.e103490.

43. Lauderdale DS, Knutson KL, Yan LL, et al. Self-reported and measured sleep duration: how similar are they? *Epidemiology*, 2008, **19**(6), pp.838-45.

44. Arora T and Taheri S. Associations among late chronotype, body mass index and dietary behaviors in young adolescents. *International Journal of Obesity (2005)*, 2015, **39**(1), pp.39-44.

45. Malone SK, Zemel B, Compher C, et al. Characteristics Associated with Sleep Duration, Chronotype, and Social Jet Lag in Adolescents. *Journal of School Nursing*, 2016, **32**(2), pp.120-31.

46. Horne JA and Ostberg O. A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *International Journal of Chronobiology*, 1976, **4**(2), pp.97-110.

47. Yoshizaki T, Komatsu T, Tada Y, et al. Association of habitual dietary intake with morningness-eveningness and rotating shift work in Japanese female nurses. *Chronobiology International*, 2018, **35**(3), pp.392-404.

48. Kanerva N, Kronholm E, Partonen T, et al. Tendency toward eveningness is associated with unhealthy dietary habits. *Chronobiology International*, 2012, **29**(7), pp.920-7.

49. Sato-Mito N, Sasaki S, Murakami K, et al. The midpoint of sleep is associated with dietary intake and dietary behavior among young Japanese women. *Sleep Medicine*, 2011, **12**(3), pp.289-94.

50. Sato-Mito N, Shibata S, Sasaki S, et al. Dietary intake is associated with human chronotype as assessed by both morningness-eveningness score and preferred midpoint of sleep in young Japanese women. *International Journal of Food Sciences and Nutrition*, 2011, **62**(5), pp.525-32.

51. Mota MC, Waterhouse J, De-Souza DA, et al. Association between chronotype, food intake and physical activity in medical residents. *Chronobiology International*, 2016, **33**(6), pp.730-9.

52. Fleig D and Randler C. Association between chronotype and diet in adolescents based on food logs. *Eating Behaviors*, 2009, **10**(2), pp.115-8.

53. Silva CM, Mota MC, Miranda MT, et al. Chronotype, social jetlag and sleep debt are associated with dietary intake among Brazilian undergraduate students. *Chronobiology International*, 2016, **33**(6), pp.740-8.

54. Patterson F, Malone SK, Lozano A, et al. Smoking, Screen-Based Sedentary Behavior, and Diet Associated with Habitual Sleep Duration and Chronotype: Data from the UK Biobank. *Annals of Behavioral Medicine*, 2016, **50**(5), pp.715-726.

55. Owens JA and Weiss MR. Insufficient sleep in adolescents: causes and consequences. *Minerva Pediatrica*, 2017, **69**(4), pp.326-336.

56. Suttorp MM, Siegerink B, Jager KJ, et al. Graphical presentation of confounding in directed acyclic graphs. *Nephrology, Dialysis, Transplantation*, 2015, **30**(9), pp.1418-23.

57. Adan A. Chronotype and personality factors in the daily consumption of alcohol and psychostimulants. *Addiction*, 1994, **89**(4), pp.455-62.

Chapter 3: Fruit and vegetable consumption and their polyphenol content are inversely associated with sleep duration: prospective associations from the UK Women's Cohort Study

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3.1 Abstract

This study aims to investigate the prospective associations between FV intakes and their polyphenol content with subsequent sleep duration in UK women. In this study, 13,958 women with ~4 years of follow-up in the UKWCS were included in the analyses. FV intakes were assessed at baseline using a FFQ and average hours of sleep per day were self-reported in follow-up. Polyphenol intake was calculated by matching FV items from the FFQ with the Phenol-Explorer database. Linear regression models, adjusting for confounders, were used for the analyses. Consuming an additional portion of apples, kiwi, oranges, pineapple, and 100% pure juice were associated with shorter sleep. Similarly, an additional portion of cabbage, celery, aubergine, olives, and peppers were inversely associated with sleep duration. An additional gram of total polyphenols was associated with shorter sleep by 18 min (99% CI -31 to -4, $p < 0.001$). FV consumption and total polyphenol content were inversely associated with sleep duration; however, effect sizes were small, and polyphenol classes from FV intakes were not associated with sleep duration. Future intervention studies considering the time of FV consumption in relation to sleep are needed to clarify the underlying mechanisms.

Keywords: sleep; fruits and vegetables; polyphenols

3.2 Introduction

Epidemiological studies have shown that short sleep duration is associated with hypertension (1), type 2 diabetes (2), cardiovascular disease (3), all-cause mortality (4,5), and a 45% increased risk of obesity compared to normal sleep duration (6,7). These associations, in part, may be mediated through changes in dietary intake including FV that influence bodyweight and chronic disease risk (8, 9). However, the directionality of these associations are not well established; a reciprocal relationship has been suggested (10, 11). Recently, St-onge et al. suggested that plant-based diets could have potential benefits for reducing cardiovascular risk by improving sleep (12). These benefits may be facilitated by dietary polyphenols that have been shown to modulate the circadian rhythms (13) and sleep-wake cycles (14) in rodents. In humans, consuming 2 kiwi fruits an hour before bedtime improved sleep onset, duration, and efficiency in 24 healthy adults during a 4-week open clinical trial (15). Furthermore, a double-blinded pilot study showed that fresh tart cherry juice reduced insomnia in 15 elderly subjects (16). The effects of cherries were also observed to increase sleep duration and reduce the number of awakenings, as measured by actigraphy in 12 Spanish participants (17). These clinical evidence studies suggest sleep-promoting effects of certain fruits;

however, they were conducted on small study groups. The limited number of longitudinal epidemiological studies in this area suggests the need for cohort studies with validated dietary intake measures to clarify this association. Therefore, the aim of this study was to explore the prospective associations between specific FV intakes and polyphenol content of FV and sleep duration in a large cohort of UK women. To our knowledge, we are the first to report on prospective associations between specific FV intakes and their polyphenol content with sleep duration using a large cohort. We hypothesized that FV intakes and their polyphenol contents are associated with longer sleep durations.

3.3 Methods

3.3.1 Participants

The UKWCS is a large prospective cohort that was established to explore links between diet and chronic diseases. Participants were taken from responders to the World Cancer Research Fund's direct mail survey including those living in England, Wales, Scotland, and Northern Ireland. Ethical approval was granted at its initiation in 1993 (Research Ethics Committee reference number is 15/YH/0027). The National Research Ethics Committee for Yorkshire and the Humber, Leeds East has now taken on responsibility for the ongoing cohort (18). Baseline data collection was between 1995 and 1998 (Figure 3.1.) using a postal FFQ. Follow-up data (Phase 2) was collected between 1999 and 2002 around 4 years later, and 14,172 women (40% of baseline) completed a follow-up health and life style questionnaire including sleep, and 12,453 women also completed a 4-day food diary and a 1-day activity diary.

3.3.2 Baseline characteristics

Age, height, weight, medical history, and smoking habits were self-reported. Physical activity was recorded using a binary question in the FFQ which questioned if participants spent time on activities vigorous enough to cause sweating or a faster heartbeat, which indicated moderate physical activity (MET-hours/day). Supplement usage was identified by asking whether participants took any vitamins, minerals, fish oils, fibre, or other food supplements. Participants also self-reported their status regarding vegetarian and vegan diets. Classification of SES was undertaken based on occupation, according to the United Kingdom NS-SEC, where women are divided into three categories (managerial/professional, intermediate, or routine/manual) (19). Socio-demographic information such as marital status was determined by self-report questions asking for marital status (married or living as married, divorced, single, widowed, or separated).

3.3.3 Fruit and vegetable intakes

Diet was assessed at baseline using a detailed 217-item FFQ developed from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Oxford cohort (20). The FFQ was validated on a subsample of 303 cohort subjects against a 4-day food diary, as well as fasting blood measures of specific nutrients (18, 21, 22). The FFQ were sent to 61,000 participants who had previously responded to a direct mail survey from the World Cancer Research Fund, and a total of 35,692 women completed the FFQ. Participants were asked to choose their frequency of consumption for each food listed in the FFQ by answering the question “how often have you eaten these foods in the last 12 months?” using one of ten response categories; never, less than once a month, 1-3 per month, once a week, 2-4 per week, 5-6 per week, once per day, 2-3 per day, 4-5 per day, and 6+ per day. These were consequently converted to weight of each food consumed per day based on the Food Standards Agency portion sizes book (23). For the current study, FV food items were used individually, and also their polyphenol contents were calculated from Phenol Explorer (24). FV consumption was expressed as grams per day (g/day); however, in order to have a better estimate, results were presented per portion size unless stated otherwise, and non-response to FV questions were taken as missing data.

3.3.4 Estimation of polyphenol intake from fruits and vegetables

The polyphenol intake was calculated by matching FV intakes from the FFQ and the recently developed Phenol Explorer database (www.phenol-explorer.eu) (24) that contains data on the content of 500 polyphenols in over 400 foods. The individual polyphenol intake from each item of FV was calculated by multiplying the content of each polyphenol by the daily consumption of each FV item. Polyphenol classes included flavonoids, phenolic acids, stilbenes, lignans, and other polyphenols (Appendix C (C.1.)). The total polyphenol intake was calculated as the sum of all polyphenol classes intake from all FV reported by the FFQ. This estimation method has been previously used in other studies (25-27). In the Phenol-Explorer database, polyphenol intake was calculated using HPLC; however, in the case of lignans and phenolic acids in some FV items (e.g., olives), polyphenol content was calculated using HPLC after hydrolysis, because these treatments are needed to release phenolic compounds that otherwise cannot be analysed (25). Polyphenol contents from FV items that were analysed using HPLC after hydrolysis are indicated in the tables.

3.3.5 Sleep duration

Participants were asked about sleep duration using the lifestyle questionnaire in phase 2 in two separate questions in the following form (Appendix C (C.2.));

“On an average weekday, how is your day spent?”

“On an average weekend, how is your day spent?”

Participants were asked to record number of hours and/or minutes that were spent sleeping in an average weekday and weekend. Two separate variables were generated for sleep duration based on weekdays and weekends for all women. Average sleep duration was calculated using the following equation (9).

((minutes slept during the week X 5) + (minutes slept during weekends X 2))/7

3.3.6 Statistical analyses

Descriptive statistics, such as means and proportions, described women from the UKWCS according to FV quintiles. We have previously reported from cross-sectional data that sleep duration and FV intakes are non-linearly associated (9). In order to use linear regression models, we assessed the relationship between FV intakes and sleep duration using locally weighted scatterplot smoothing (LOWESS) (28), which is a tool that creates a smooth line through a scatterplot to help see the trend between variables. The association between total FV intakes (grams/day) and sleep duration (hours/day) showed a linear association (Appendix C (C.3.)). Normal distribution of the outcome variable (sleep duration) was checked using histogram plot (Appendix C (C.4.)).

Linear regression models were used to assess the prospective association between FV intakes (continuous exposure in grams/day) or their polyphenols (continuous exposure) and sleep duration (continuous outcome in minutes/day). Unadjusted and adjusted models were used where potential confounders were identified based on previous studies (9). Confounders were age, SES (professional and managerial, intermediate, routine and manual), smoking (yes, no), ethnicity (white, Bangladeshi, Indian, Chinese, Pakistani, black-Caribbean, black-other, other) and total energy intake. Models that investigated polyphenol intake from FV and sleep duration were further adjusted for other polyphenol content; for example, flavonoids were adjusted for phenolic acids, stilbenes, lignans, and other polyphenols. Total polyphenol intake in association with sleep duration was adjusted for the confounders mentioned above without further adjustment of other polyphenol content. There is not sufficient experimental evidence that body mass index

(BMI) and physical activity independently influence FV consumption and their polyphenols to include as an adjustment in the main analyses; however, there is evidence of BMI influencing sleep duration. We adjusted for BMI and physical activity but it did not meaningfully change the results; therefore, the results are shown without adjusting for these covariates. The final number (n column in Tables 3.2-3.4 and in Appendix C (C.5- C.10)) of women included in the analyses indicates complete data of all covariates included in the model, and difference in (n) is due to missing data of any of the included covariates in the model.

Sensitivity analyses were conducted on polyphenol content from FV intakes since they are unstable compounds and can be affected by alcohol intake, supplement use, and medications (29). Sensitivity analyses included stratifications of certain variables selected prior to analyses between polyphenol content from FV and sleep duration. Variables explored were alcohol consumption frequency (more than once a week, once a week or less, never), BMI (obese vs. non-obese), and dietary habits (vegetarian/vegan vs. non-vegetarian/vegan). Separate analyses were conducted after excluding 1) supplement users, 2) those who self-reported currently having a longstanding illness (see Appendix C (C.9.) for excluded illnesses), and 3) those who self-reported taking prescribed medicines. Further sensitivity analyses included considering weekdays and weekends sleep duration separately, since sleep and dietary habits differ between weekdays and weekends (controlled for confounders stated above in the adjusted model). Further adjustment for BMI and physical activity (MET/hours) in the adjusted model stated above was conducted. To take account of multiple testing, significance level was determined by a p value of <0.01 to reflect 99% confidence intervals in main and sensitivity analyses. All analyses were conducted using Stata V. 15.1 statistical software (StataCorp LLC, College Station, TX, USA) (30).

3.4 Results

3.4.1 Socio-Demographic Characteristics

Cohort participants who had unavailable data on sleep duration, extreme sleep duration <2 and >12 h/day, pregnant women, and those with extreme total energy intake <500 and >6000 were excluded, and a total of 13,958 women were included in the analyses (Figure 3.1.). Baseline characteristics of the participants based on FV quintiles are shown in Table 3.1. The mean age was 52 years (95% CI 52 to 53), and mean BMI was 24.5 (95% CI 24.4 to 24.5). Women had on average 7.5 h/day of sleep (95% CI 7.5 to 7.6) and 24 min/day (95% CI 23 to 25) of physical activity. In total, 32% (95% CI 31 to 32) of women were vegetarian or vegan, 98% (95% CI 98 to 99) were white, and 60% (95% CI 59 to 61) reported supplement usage.

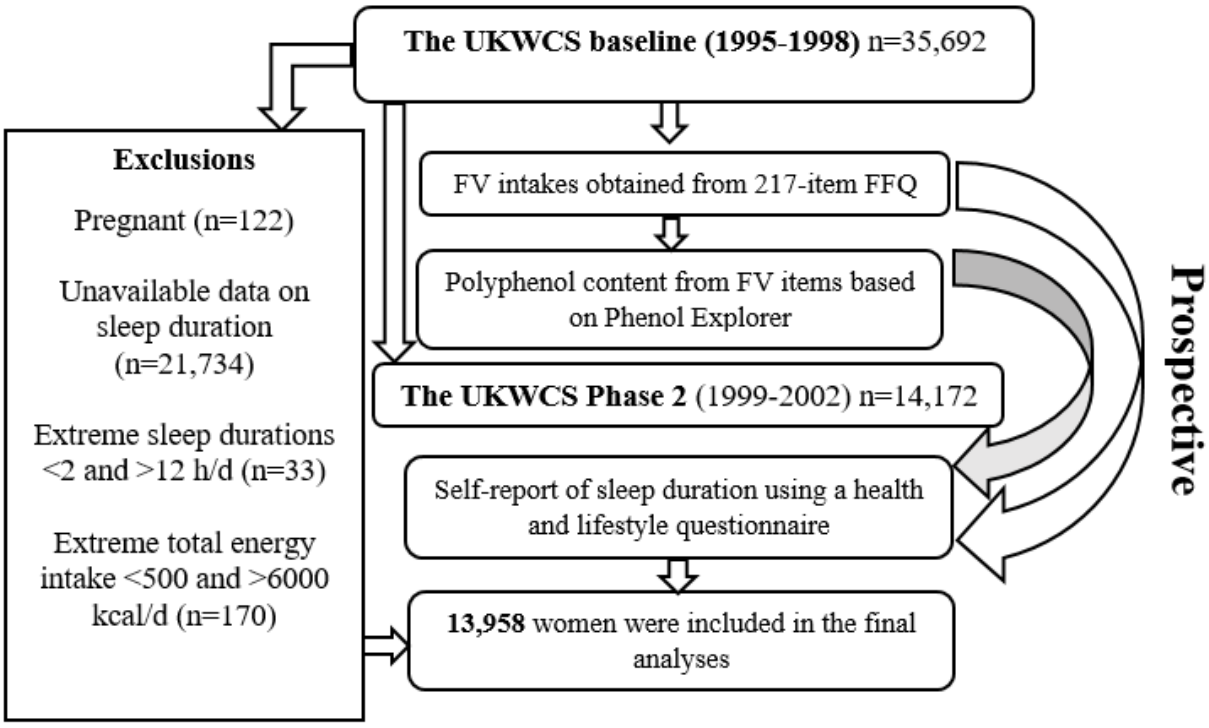

Figure 3.1. Participants flow chart.

d (day), FFQ (food frequency questionnaire), FV (fruits and vegetables), h (hours), UKWCS (The UK Women's Cohort Study).

Table 3.1. Baseline characteristics by quintile of total FV intakes.

Total FV intakes (g)	0-348	348-486	486-624	624-817	817-1597	Total
Number of women (n)	**2,364**	**2,710**	**2,873**	**2,996**	**3,015**	**13,958**
Characteristics	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**
Age (years)	51 (50, 51)	52 (51,52)	52 (52 ,52)	52 (52,52)	53 (52,53)	52 (52,53)
BMI (kg/m^2)	24.4 (24.2,24.5)	24.1(24.0,24.3)	24.2 (24.0,24.3)	24.0 (23.9,24.2)	24.1 (23.9,24.2)	24.5(24.4,24.5)
Total energy intake (kcal/day)	2036 (2004,2069)	2115 (2092,2138)	2272 (2249,2295)	2422 (2398,2446)	2698 (2672,2724)	2307 (2299,2314)
Sleep duration*	7.5 (7.5,7.6)	7.5 (7.5,7.6)	7.5 (7.5,7.5)	7.5 (7.5,7.6)	7.4 (7.4,7.5)	7.5 (7.5,7.6)
Weekday sleep duration*	7.5 (7.4,7.5)	7.5 (7.5,7.5)	7.5 (7.4,7.5)	7.5 (7.4,7.5)	7.4 (7.4,7.4)	7.5 (7.4,7.5)
Weekend sleep duration*	7.9 (7.9,8.0)	7.9 (7.9,7.9)	7.9 (7.8,7.9)	7.9 (7.8,7.9)	7.7 (7.7,7.8)	7.9 (7.8,7.9)
Physical activity (minutes/day)	27 (24,29)	21 (20,22)	23 (21,24)	23 (22,24)	28 (26,29)	24 (23,25)
	% (95% CI)	**% (95% CI)**	**% (95% CI)**	**% (95% CI)**	**% (95% CI)**	**% (95% CI)**
Has longstanding illness (yes)	25 (23, 27)	24 (23,26)	26 (24,28)	27 (25,28)	28 (26,29)	26 (25,27)
Prescribed medicine (yes)	31.2 (29, 33)	32.1 (30,33)	30.6 (28,32)	31.8 (30,33)	31.8 (30,33)	31.5 (30,32)
Smoking (yes)	13 (12, 14)	9 (8,10)	8 (7,9)	6 (5,7)	6 (5,7)	8 (8,9)
Supplement use (yes)	55 (53,57)	56 (54,57)	59 (56, 60)	62 (60,63)	67 (65, 69)	60 (59,61)
Vegetarian or vegan(yes)	24 (22,26)	27 (25, 28)	30 (28, 31)	34 (33,36)	42 (40,43)	32 (31,32)
Ethnicity (white)	98 (98,99)	99 (98,99)	99 (98,99)	98 (98, 99)	98 (97, 98)	98 (98,99)
Employer (employed)	62 (60,63)	60 (58,62)	59 (57, 61)	58 (56,60)	56 (54,57)	59 (58,60)
SES (professional)	61 (59,63)	63 (61,65)	67 (65,69)	67 (65, 68)	70 (68,71)	66 (65,66)
Marital status (married)	73 (71,75)	75 (74,73)	77 (75,78)	77(75,78)	77 (75,78)	76 (75,77)
Number of children (2 children)	51 (49,54)	52 (50,54)	51 (49,53)	48 (46,51)	49 (47,51)	49,51)

Legend: BMI (body mass index) CI (confidence interval), FV (fruits and vegetables), mg (milligram), µg (microgram), m (metre), SES (socio-economic status).
*Hours/day

3.4.2 Prospective associations between individual FV items and sleep duration

In adjusted models (Table 3.2.), consuming an additional portion of the following fruits were associated with shorter sleep: apples 2 minutes/day (99% CI -4 to -1, p<0.001), kiwi 10 minutes/day (99% CI -19 to -2, p=0.001), oranges 3 minutes/day (99% CI -5 to 0.8, p<0.001), pineapple 17 minutes/day (99% CI -33 to -1, p=0.006) and 100% pure juice 3 minutes/day (99% CI -3 to -0.07, p=0.001). Similarly, consuming an additional portion of the following vegetables were associated with shorter sleep: cabbage 6 minutes/day (99% CI -12 to -0.4,p= 0.006), celery 12 minutes/day (99% CI -23 to -0.5,p=0.007), aubergine 21 minutes/day (99%CI -41 to -1, p=0.007), olives 37 minutes/day (99% CI -71 to -3, p=0.004) and peppers 13 minutes/day (99% CI -23 to -3, p=0.001).

Table 3.2. The prospective associations between FV items and sleep duration.

Sleep duration (minutes/day)						
Models	**Unadjusted**			**Adjusted***		
Fruit	**Coefficient per additional 80 g/day (99% CI)**	**P value**	**n**	**Coefficient per additional 80 g/day (99% CI)**	**P value**	**n**
Apples	-2 (-4,-1)	<0.001	13,530	-2 (-4,-1)	**<0.001**	12,862
Avocados	-8 (-22,4)	0.1	8,468	-8 (-23,5)	0.1	8,033
Bananas	-0.4 (-2,1)	0.5	13,092	-0.6 (-2,1)	0.4	12,437
Grapes	-1 (-4,0.5)	0.05	13,312	-1 (-3,1)	0.2	12,664
Kiwi	-10 (-19,-2)	0.001	11,709	-10 (-19,-2)	**0.001**	11,147
Mangoes	-6 (-16,4)	0.1	7,293	-6 (-17,4)	0.1	6,930
Oranges, satsumas	-2 (-4,0.4)	0.002	12,967	-3 (-5,-0.8)	**<0.001**	12,330
Papaya	-4 (-18,9)	0.4	3,646	-5 (-20,9)	0.3	3,445
Pears	-0.3 (-3,2)	0.7	12,177	-0.1 (-3,2)	0.8	11,576
Pineapple	-20 (-35,-4)	0.001	11,810	-17 (-33,-1)	**0.006**	11,243
Apricots	-44 (-89,1)	0.01	11,010	-40 (-88,6)	0.02	10,456
Melon	-1 (-4,0.8)	0.07	13,110	-1 (-4,1)	0.2	12,478
Nectarines	-3 (-26,19)	0.6	12,678	-8 (-32,14)	0.3	12,062
Peaches	-32 (-71,6)	0.03	12,945	-32 (-73,8)	0.04	12,315
Plums	-29 (-74,16)	0.09	12,839	-31 (-77,15)	0.08	12,217
Raspberries	-4 (-14,6)	0.2	12,643	-2 (-13,7)	0.4	12,040
Red/black currants,	-4 (-12,2)	0.09	10,426	-4 (-11,3)	0.1	9,910
Rhubarb	1 (-2,4)	0.3	11,359	1 (-2,4)	0.3	10,829
Strawberries	-12 (-31,6)	0.09	13,321	-11 (-31,8)	0.1	12,673
Orange juice per 125 g/d	-1 (-3,0.5)	0.06	12,224	-1 (-3,0.4)	0.04	11,642
100% pure fruit juice per 125 g/d	-3 (-6, -0.08)	0.001	10,345	-3 (-6,-0.07)	**0.001**	9,834

Table 3.2. (continued) The prospective associations between FV items and sleep duration.

	Sleep duration (minutes/day)					
	Unadjusted			Adjusted*		
	Coefficient per additional 80 g/day (99% CI)	P value	n	Coefficient per additional 80 g/day (99% CI)	P value	n
Dried fruit						
Dates	-2 (-8,3)	0.2	9,577	-3 (-9,3)	0.1	9,117
Figs	-0.008 (-3,3)	0.9	7,231	-0.2 (-3,3)	0.8	6,860
Prunes	-4 (-11,2)	0.09	9,205	-4 (-11,2)	0.1	8,739
Mixed dried fruit	-0.9 (-6,4)	0.6	8,972	-0.8 (-6,4)	0.6	8,531
Currants, raisins, sultanas	0.4 (-6, 7)	0.8	12,605	0.8 (-6,8)	0.7	12,003
Vegetables						
Beetroot	-16 (-35,1)	0.01	11,516	-12 (-31,7)	0.1	10,951
Broccoli, spring greens, kale	-2 (-7,1)	0.1	13,488	-1 (-6,3)	0.5	12,822
Brussels	-3 (-9,2)	0.1	12,783	-0.6 (-7,6)	0.8	12,153
Cabbage	-8 (-13,-3)	<0.001	13,051	-6 (-12,-0.4)	**0.006**	12,425
Carrots	-2 (-7,2)	0.1	13,713	-1 (-6,3)	0.5	13,037
Cauliflower	-0.04 (-0.1,0.01)	0.06	13,503	-0.03 (-0.1,0.03)	0.2	12,842
Celery	-14 (-25,-3)	0.001	12,483	-12 (-23,-0.5)	**0.007**	11,865
Coleslaw	-6 (-27,15)	0.4	10,018	-4 (-27,17)	0.5	9,546
Courgettes, marrow, squash	-6 (-14,2)	0.05	11,697	-7 (-16,1)	0.03	11,134
Cucumber	-17 (-32,-1)	0.005	12,911	-15 (-32,0.8)	0.01	12,293
Green/ runner beans	-6 (-11,-1)	0.001	13,344	-5 (-10,0.6)	0.02	12,688
Lettuce	-15 (-31,-0.1)	0.009	13,550	-14 (-30,2)	0.02	12,885
Aubergine, okra	-25 (-44,-6)	<0.001	8,258	-21 (-41,-1)	**0.007**	7,853
Olives	-36 (-69,-3)	0.005	6,461	-37 (-71,-3)	**0.004**	6,129
Parsnips	-0.7 (-12,10)	0.8	11,704	1 (-19,13))	0.6	11,137
Peas	-5 (-15,3)	0.1	13,132	-5 (-15,4)	0.1	12,510
Peppers	-10 (-20,-1)	0.004	12,371	-13 (-23,-3)	**0.001**	11,780
Swedes	-0.07 (-11,11)	0.9	11,052	1 (-10,13)	0.7	10,512
Tomatoes	-2 (-5,0.1)	0.01	13,526	-2 (-5, 0.1)	0.01	12,872
Turnip	-5 (-20,9)	0.3	8,998	-5 (-21,10)	0.3	8,568
Mustard, cress, watercress	-21 (-73,31)	0.3	11,283	-21 (-75,32)	0.3	10,736
Boiled/mashed potatoes	0.3 (-1,1)	0.5	13,330	0.9 (-0.6,2)	0.1	12,692

* Adjusted for age, socio-economic status, smoking, ethnicity and total energy intake

3.4.3 Prospective associations between total polyphenol content from FV and sleep duration

Table 3.3. shows the prospective associations between total polyphenol intake from FV and sleep duration. In unadjusted analyses (Table 3.3.), an additional gram of flavonoids, lignans, other polyphenols and total polyphenols were inversely associated with sleep duration ($p<0.01$). In adjusted analyses (Table 3.3.), an additional gram of total polyphenols was associated with shorter sleep by 18 minutes (99% CI -31 to -4, $p<0.001$).

Table 3.3. The prospective associations between total polyphenols from FV consumption and sleep duration.

Sleep duration (minutes/day)						
	Unadjusted			Adjusted*		
Polyphenol class	**Coefficient per additional gram (99% CI)**	**P value**	**n**	**Coefficient per additional gram (99% CI)**	**P value**	**n**
Total flavonoids	-30 (-54, -6)	0.001	13,636	-30 (-61,1)	0.01	12,816
Total phenolic acids	-22 (-61,17)	0.1	13,635	22 (-30,74)	0.2	12,816
Total other polyphenols	-180 (-330,-30)	0.002	13,805	-136 (-299,27)	0.03	12,816
Total stilbenes	-4011 (-8731,708)	0.03	13,670	-538 (-6418,5341)	0.08	12,816
Total lignans	-28 (-54,-2)	0.005	13,880	-14 (-43,15)	0.2	12,816
Total polyphenols from FV**	-16 (-28,-5)	<0.001	13,636	-18 (-31,-4)	0.001	12,971

Legend: FV (fruits and vegetables).
*Adjusted for age, socio-economic status, smoking, ethnicity, total energy intake and other polyphenol components.
**Total polyphenols (not adjusted for other polyphenol components) = the sum of total flavonoids, total phenolic acids, total other polyphenols, total stilbenes and total lignans.

3.4.4 Prospective associations between polyphenol classes from FV items and sleep duration

Table 3.4. shows the prospective associations between polyphenol classes from FV and sleep duration. In unadjusted analyses (Table 3.4.), flavonoids from apples, kiwi, oranges cabbage, cucumber, green beans, lettuce, olives and peppers were negatively associated with sleep duration. Phenolic acids from lettuce, aubergine, olives and peppers were also negatively associated with sleep duration. Other polyphenols from

celery and olives were negatively associated with sleep duration. Lignans from oranges, cabbage and cucumber were negatively associated with sleep duration.

In adjusted analyses (Table 3.4.), an additional mg of flavonoids from apples was associated with 0.5 minutes/day shorter sleep (99% CI -0.8 to-0.1, p<0.001), an additional mg of flavonoids from oranges was associated with 0.08 minutes/day shorter sleep (99% CI -0.1, -0.01, p=0.002), an additional mg of flavonoids from peppers was associated with 3 minutes/day shorter sleep (995% CI -0.6, -0.4,p = 0.003) and an additional mg of phenolic acids from peppers were associated with 31 minutes/day shorter sleep (99% CI -60 to -2, p = 0.005).

Table 3.4. The prospective associations between polyphenol classes from FV consumption and sleep duration.

	Sleep duration (minutes/day)					
	Unadjusted			Adjusted*		
Polyphenol classes	**Coefficient per additional mg (99% CI)**	**P value**	**n**	**Coefficient per additional mg (99% CI)**	**P value**	**n**
Flavonoids						
Apple	-0.5 (-0.8,-0.2)	<0.001	13,530	-0.5 (-0.8,-0.1)	**<0.001**	12,536
Avocados	-19 (-50,11)	0.1	8,468	-7 (-41, 26)	0.5	7,900
Banana	-0.1 (-0.6,0.4)	0.5	13,092	-0.1 (-0.7,0.4)	0.5	12,115
Grape	-0.3 (-0.8,0.1)	0.05	13,312	-0.001 (-0.5, 0.5)	0.9	12,413
Kiwi	-19 (-34, -5)	0.001	11,709	-15 (-31, 0.8)	0.02	10,939
Mangoes	-4 (-11,2)	0.1	7,293	-1 (-9,7)	0.6	6,831
Oranges **	-0.07 (-0.13,0.01)	0.002	12,967	-0.08 (-0.1, -0.01)	**0.002**	12,054
Pears	-0.09 (-0.81,0.62)	0.7	12,177	0.1 (-0.6,0.9)	0.5	11,352
Apricots	-7 (-14,0.3)	0.01	11,010	-4 (-12,4)	0.2	10,304
Nectarines	-0.3 (-2,1)	0.6	12,678	-0.3 (-2, 1)	0.6	11,824
Peaches	-17 (-38,3)	0.03	12,945	-13 (-39,11)	0.1	12,063
Plums	-0.3 (-0.9,0.2)	0.09	12,839	-0.3 (-1,0.2)	0.1	11,981
Raspberries	-0.05 (-0.1,0.08)	0.2	12,643	-0.03 (-0.2, 0.1)	0.6	11,815
Redcurrants	-0.1 (-0.3, 0.08)	0.09	10,426	-0.02 (-0.6,0.5)	0.9	9,784
Rhubarb	0.4 (-0.81, 1)	0.3	11,359	0.9 (-0.4,2)	0.09	10,620
Strawberries	-0.1 (-0.4, 0.1)	0.09	13,321	-0.1 (-0.4,0.2)	0.4	12,433
Orange juice	-0.02 (-0.06,0.01)	0.06	12,224	-0.01 (-0.05,0.02)	0.3	12,054
Figs	-0.2 (-121, 120)	0.9	7,231	-6 (-141,127)	0.8	6,739
Prunes	-7 (-17, 3)	0.09	9,205	-8 (-21,4)	0.08	8,565
Raisins	3 (-49, 56)	0.8	12,605	6 (-52,64)	0.7	11,726
Beetroot**	-42 (-87,3)	0.02	11,516	-27 (-77,22)	0.1	10,681
Broccoli	-0.1 (-0.3,0.08)	0.1	13,488	-0.01 (-0.2,0.2)	0.8	12,490
Brussels**	-3 (-8,2)	0.1	12,783	0.8 (-5,7)	0.7	11,846
Cabbage **	-262 (-431,-93)	<0.001	13,051	-180 (-373,11)	0.02	12,107
Cucumber**	-209 (-403,-15)	0.005	12,911	-165 (-372,41)	0.04	12,002
Green beans	-1 (-1,-0.2)	0.001	13,344	-0.4 (-1, 0.4)	0.1	12,363
Lettuce	-4 (-9,-0.03)	0.009	13,550	-3 (-8,1)	0.07	12,555
Olives	-0.2 (-0.5,-0.02)	0.005	6,461	1 (-0.8,2)	0.1	6,049
Parsnips **	-0.9 (-15,13)	0.8	11,705	4 (-11,19)	0.4	10,885
Peas	-356 (-939,226)	0.1	13,132	-272 (-908,364)	0.2	12,195
Peppers	-3 (-5,-0.3)	0.004	12,371	-3 (-6,-0.4)	**0.003**	11,527
Swedes **	-0.01 (-2,2)	0.9	11,052	0.4 (-1,2)	0.6	10,268

Table 3.4. (continued) The prospective associations between polyphenol classes from FV consumption and sleep duration.

	Sleep duration (minutes/day)					
	Unadjusted			Adjusted*		
	Coefficient per additional mg (99% CI)	P value	n	Coefficient per additional mg (99% CI)	P value	n
Tomatoes	-10 (-22,0.5)	0.01	13,526	-8 (-20,4)	0.08	12,534
Watercress **	-1 (-6,2)	0.3	11,283	-0.6 (-5, 4)	0.7	10,531
Phenolic acids						
Bananas	-0.5 (-3,2)	0.5	13,092	-0.2 (-3,2)	0.8	12,115
Grapes (green)	-0.2 (-0.4, 0.06)	0.05	13,312	-0.008 (-0.3, 0.3)	0.9	12,413
Pears	-0.03 (-0.3,0.2)	0.7	12,177	0.1 (-0.1, 0.4)	0.3	11,352
Apricots	-5 (-11,0.2)	0.01	11,010	-2 (-9, 3)	0.2	10,304
Nectarines	-0.4 (-3,2)	0.6	12,678	0.2 (-3, 3)	0.8	11,824
Peaches	-1 (-3,0.3)	0.03	12,945	-0.7 (-3, 1)	0.4	12,063
Plums	-0.4 (-1,0.2)	0.09	12,839	-0.2 (-0.9, 0.5)	0.4	11,981
Raspberries	-0.04 (-0.1,0.06)	0.2	12,643	0.03 (-0.1, 0.1)	0.5	11,815
Redcurrants	-2 (-5,1)	0.09	10,426	-0.2 (-7,7)	0.9	9,784
Strawberries	-1 (-3,0.6)	0.09	13,321	-0.1 (-2,2)	0.9	12,433
Dates	-0.4 (-1,0.5)	0.2	9,577	-0.3 (-1,0.7)	0.4	8,942
Prunes	-0.09 (-0.2,0.04)	0.09	9,205	-0.07 (-0.2,0.07)	0.2	8,565
Raisins	0.1 (-1,2)	0.8	12,605	0.3 (-1,2)	0.6	11,726
Broccoli	-0.1 (-0.5, 0.1)	0.1	13,488	0.05 (-0.3,0.4)	0.6	12,490
Carrots	-0.1 (-0.4, 0.1)	0.1	13,713	-0.03 (-0.3,0.3)	0.7	12,679
Phenolic acids						
Cauliflower	-0.6 (-1, 0.2)	0.06	13,503	-0.2 (-1,0.8)	0.5	12,509
Lettuce	-5 (-10,-0.03)	0.009	13,550	-3 (-9,2)	0.1	12,555
Aubergine	-21 (-36,-5)	<0.001	8,258	-14 (-31,2)	0.03	7,735
Olives	-0.3 (-0.6,-0.02)	0.005	6,461	-0.5 (-3,2)	0.6	6,049
Peppers	-29 (-55,-3)	0.004	12,371	-31 (-60,-2)	**0.005**	11,527
Tomatoes	-0.8 (-1, 0.04)	0.01	13,526	-0.4 (-1,0.4)	0.2	12,534
Potatoes	0.01 (-0.04,0.07)	0.5	13,330	0.04 (-0.02,0.1)	0.1	12,346
Other polyphenols						
Pears	-9 (-78,60)	0.7	12,177	28 (-47,103)	0.3	11,352
Orange juice	-0.5 (-1,0.2)	0.06	12,224	1 (-0.02,2)	0.01	11,418
Celery	-6 (-12,-1)	0.001	12,483	-4 (-10,0.8)	0.02	11,623
Olives	-0.1 (-0.3,-0.01)	0.005	6,461	-0.1 (-0.3,0.02)	0.03	6,049
Stilbenes						
Grapes	-7 (-17,2)	0.05	13,312	-1 (-13,10)	0.7	12,413
Redcurrants	-3 (-9,2)	0.09	10,426	-0.1 (-7,6)	0.9	9,784
Strawberries	-44 (-114,24)	0.09	13,321	-15 (-98,67)	0.6	12,433
Lignans						
Oranges **	-0.2 (-0.4,-0.03)	0.002	12,967	-0.2 (-0.4, 0.05)	0.03	12,054
Pineapple**	-0.1 (-0.2,-0.02)	0.001	11,810	-0.09 (-0.2,0.004)	0.01	11,027
Melon*	-0.02 (-0.05,0.009)	0.07	13,110	-0.005 (-0.04,0.02)	0.6	12,195
Brussels**	-0.06 (-0.1,0.04)	0.1	12,783	0.006 (-0.1,0.1)	0.9	11,846
Cabbage **	-132 (-218,-47)	<0.001	13,051	-89 (-185,6.8)	0.01	12,107
squash**	-862 (-2011,287)	0.05	11,697	-874 (-2124,375)	0.07	10,914
Cucumber**	-5 (-10,-0.4)	0.005	12,911	-4 (-9,0.9)	0.03	12,002
Parsnips **	-19 (-303,264)	0.8	11,705	70 (-233, 374)	0.5	10,885
Swedes **	-19 (-2822, 2783)	0.9	11,052	434 (-2671,3539)	0.7	10,268
Turnip **	-45 (-173, 83)	0.3	8,998	-57 (-194, 80)	0.2	8,381

*Adjusted for age, socio-economic status, smoking, ethnicity, total energy intake and other polyphenol components.
**Analysed using chromatography after hydrolysis.

3.4.5 Sensitivity analyses

Sensitivity analyses showed broadly similar results (Appendix C (C.5.-C.10). Analyses between polyphenol content from FV and sleep duration stratified by BMI (<25 kg/m2 vs. ≥25 kg/m2) showed that an additional gram of total polyphenols were associated with shorter sleep by 20 min/day (99% CI -36 to -4, p = 0.001) in women with a BMI <25 kg/m2, whereas no association was observed in women with a BMI ≥25 kg/m2 (Appendix C (C.5.)). Stratification of analyses by vegetarian/vegan status showed that an additional gram of total flavonoids were associated with shorter sleep by 52 min/day (99% CI -92 to -13, p = 0.001) and total polyphenols by 18 min/day (99% CI -35 to -1, p = 0.006) in non-vegan/vegetarian women (Appendix C (C.6.)). When considering weekday and weekend sleep duration separately (Appendix C (C.7.), total polyphenol intakes were negatively associated with sleep duration on both weekdays and weekends. Analyses between FV intakes and sleep duration stratified by frequency of alcohol consumption showed that total flavonoids from FV were associated with shorter sleep by 44 min/day (99% CI -89 to -0.7, p = 0.009) in women consuming alcohol more than once a week (Appendix C (C.8.)). Similarly, total polyphenols from FV were associated with shorter sleep by 23 min/day (99% CI -45 to -2, p = 0.005) in women consuming alcohol once a week or less.

After excluding women who reported supplement intake, results were attenuated and no association was found between polyphenol intakes and sleep duration (Appendix C (C.9.)) although not significant, polyphenol intakes tended to be negatively associated with sleep duration. After excluding women who reported having a long-term illness, an additional gram of total polyphenols from FV were associated with 18 min/day shorter sleep (99% CI -34 to -3, p = 0.001) (Appendix C (C.9.)) and after excluding women who reported medication use, other polyphenols were negatively associated with sleep duration (Appendix C (C.9.)). Results were attenuated between polyphenol intakes and sleep duration after further adjustment of BMI and physical activity (Appendix C (C.10.)) however, the associations tended to be negative.

3.5 Discussion

To our knowledge, this is the first study to report prospective associations between specific FV items and their polyphenol content with sleep duration in a large cohort of UK women. A total of 13,958 women were followed up for approximately 4 years and were included in this study. Our results showed that intakes of apples, kiwi, oranges,

pineapple, 100% pure juice, cabbage, celery, cucumber, aubergine, olives, peppers, tomato, and total FV were associated with shorter sleep. In terms of polyphenol content, total polyphenols from FV were negatively associated with sleep duration. Flavonoids from apples, oranges, and peppers were associated with shorter sleep, and phenolic acids from peppers were associated with shorter sleep. Collectively, these findings suggest that among UK women, specific FV items, and total polyphenol intake from FV were associated with shorter sleep. This was not what we had anticipated from previous, smaller scale studies (15-17).

Our results are in contrast to some human studies; for example, tart cherry juice has been shown to reduce insomnia severity in older adults in a pilot study (16). However, no improvement was observed in sleep latency, duration, or efficiency; this may be due to the small sample size (n = 15) and the short period of intervention (2 weeks). In addition, the consumption of cherry increased sleep duration and 6-sulfatoxymelatonin (a metabolite that is considered to reflect the nocturnal melatonin concentration) concentrations in the urine in middle aged and elderly participants (17). However, this study also had a small sample size (n = 12) and short period of intervention (3 days). Similarly, the consumption of 2 kiwifruits 1 h before bedtime for 4 weeks increased sleep duration by 13% in adults reporting sleep disturbances (15). In our results, an additional portion of kiwi intake was associated with 10 min/day shorter sleep (99% CI -19 to -2, p = 0.001).

Furthermore, in regard to polyphenol intake and sleep, a recent study investigated the effects of chronic supplementation of Holisfiit®, a polyphenol-rich extract-based food supplement developed from FV, on both body composition and subjective perception of mental and physical health in 33 overweight and obese participants (31). After 16-week of supplementation, awakening during the night, total sleep duration, and sleep quality improved by 38% (p = 0.04), 50% (p = 0.02) and 43% (p = 0.03), respectively. In this study, total polyphenol intake was associated with shorter sleep. However, it is important to note that Holisfiit® provided bioactive compounds of polyphenols from flavonoids, delivering flavanones, anthocyanins, and flavanols, and natural components of the methylxanthine family from both an extract of green tea and an extract of yerba mate leaves as well as vitamin B3. Polyphenol effects from supplements differ in bioavailability (32) and concentration to polyphenols from foods (33), which may be one explanation of our different results. Furthermore, a considerable amount of evidence is supporting the hypothesis that high-dose polyphenols from supplements can cause adverse effects

through pro-oxidative action, whereas the risk of toxicity from food is low due to poor absorption (33). Since polyphenols are unstable compounds, some factors need to be considered in comparing our results with previous studies, such as food processing, storage, and ripening stage that impact dietary polyphenol composition (29). Furthermore, polyphenol content between foods is highly variable, and even within a specific food item the polyphenol content may vary (33). These conflicting results may be due to the different study designs and participants. Experimental trials on participants with sleep problems differ from healthy free-living individuals; therefore, it is required to consider the potential for non-representative samples taking part in experimental studies.

Our findings are in line with one animal study by Pifferi et al. (14). They tested the effects of resveratrol dietary supplement, a dietary polyphenolic compound present in FV, on non-human primate grey mouse lemur sleep-wake cycle. After three weeks of resveratrol supplementation, the animals exhibited a significantly-increased proportion of active-wake time occurring during the resting phase (light) of the sleep-wake cycle. Negligible changes in active-wake time during the active phase (dark) of the sleep wake cycle suggesting that resveratrol activity depends largely on the time of administration. Dosing-time dependency of polyphenols were shown previously on melatonin levels (34), the expression pattern of clock genes in the hypothalamus of rats (34), rat tissue lipoperoxidation (35), and adjustment of the clock system in rat liver (36). Resveratrol administration on male rats behaved as an antioxidant during the night and as a pro-oxidant during day-time (35).

GSPEs extract treatment maintained nocturnal melatonin levels and modulated the circadian rhythms when it was administered at the start of the day, rather than at night, in rats (34). Similarly, GSPEs modulated the molecular clock by repressing nicotinamide phosphoribosyltransferase (Nampt)—a gene that undergoes transcription by the enhancement of CLOCK—when the lights were turned on, and overexpressed when the lights were turned off, in rat livers (36). The effectiveness of polyphenols during periods of the day could be due to the discrepant functionality of the hypothalamus SCN. It has been shown that SCN cells are extensively coupled during the day, when the cells exhibit synchronous neural activity, but minimally coupled during the night, when the cells are electrically silent (34, 37).

Although the timing of FV intakes was not assessed in this study, this could be one explanation of the negative associations we found between FV intakes and sleep duration. FV intake during the day may have a different effect on sleep to when

consumed at night. However, as rats are nocturnal animals, in contrast to humans who are diurnal, assessing the zeitgeber time when polyphenol rich foods can entertain circadian rhythms and sleep measures in humans is necessary by conducting interventional trials to determine if there is a time-dependency effect of FV intakes on sleep duration.

Several potential pathways and mechanisms explain the associations between FV intake and their polyphenol content with sleep duration. One of the functions of sleep is to protect the body against the effects of free radicals produced by a high metabolic rate during waking hours (14). A study suggested that during sleep, metabolic rate and brain temperature are lower than during awake time; this may provide an opportunity to renew the enzymes affected by free radicals. Thus, foods with antioxidant effects are expected to affect the regulation of sleep measures (14). The action of FV intakes and their polyphenols on sleep measures could be by their improvement on mitochondrial function and energy metabolism by decreasing fat mass, which may lead to changes in sleep (14).

The negative associations between FV intakes and sleep duration in this study could be due to the high antioxidant content in FV that contributes to a decrease in the production of free radicals, and may lead to lower requirements of sleep (14). It is important to note that the UKWCS contains a higher proportion of vegetarians and well-educated participants, who tend to eat more healthily than the general population; thus, results need to be carefully interpreted. Since the metabolic state of a cell is coupled to the molecular clock, diet may modify rhythmic cellular activities (38). In light of this, another proposed pathway of how antioxidants may affect sleep is through the protective activation of hormetic, involving proteins such as ion channels, kinases, deacetylases, and transcription factors which regulate the expression of genes that encode cytoprotective enzymes (39)-pathways that promote SIRT1 protein expression (40). SIRT1 has a central role for reactive oxygen species mainly produced as a consequence of mitochondrial functions (41). It has been identified that several polyphenols, such as resveratrol, act as dietary activators of SIRT1 (40). In turn, SIRT1 modulates transcription factors including PER 2 (42), which are circadian clock genes that regulate the daily rhythms of locomotor activity, metabolism, and behaviour. Additionally, SIRT1 modulates the ventromedial hypothalamic clock, a brain region that contains neuronal food-synchronized clocks that contribute to regulation of the circadian rhythm in feeding behaviour (43).

Alternatively, polyphenols could adjust the central clock at intestinal levels through the gut-brain axis (34). Researchers have related the bi-directional interactions between the central nervous system, the enteric nervous system, and the gastrointestinal tract to the prominent role of the gut microbiota in these gut-brain interactions (44). The bi-directional relationship between microbiota and the circadian system have been shown in germ-free mice that have altered clock gene expression (45, 46). In light of the bi-directional relationship of the gut-brain axis, the polyphenols in FV may affect sleep through nocturnal secretion of melatonin by the pineal gland which is directly controlled in the brain by the SCN. It has been shown that GSPEs administration increased plasma melatonin levels in the middle of the light period, maintaining similar levels at dusk in Male Wistar rats (34). The beneficial effects of polyphenols may be controlled by the specific microbiota composition of each individual, and there is a strong inter-individual variability in polyphenol bioconversion by the gut microbiota (47). Some studies suggest that polyphenols have the capacity to alter the gut microbiota composition by increasing the population of beneficial microflora in the gut (48). It has been previously reported that the bioavailability of polyphenols and the presence of bioactive metabolites in rat plasma depend on the rat sex and the amount ingested (49). Recently, diverse effects of resveratrol in induced colitis in mice depended on the sex of the animal (50). Our studies included only women, and further human studies are needed to confirm if the effects of FV intakes and their polyphenols differ by sex.

Although several mechanisms have been proposed on how FV intakes and their polyphenols may affect sleep and the circadian system, more studies are needed to define the mechanisms by which polyphenols could adjust sleep measures and the central clock. Future studies that can demonstrate that the effects mediated by polyphenol supplements mimic the effects of whole foods are essential. Furthermore, dose-response and time of administration-response studies allowing for identification of the most effective doses and times are needed. Studies demonstrating that some polyphenols are transported to the brain or are present in the circulation at the times of the beneficial effects on sleep measures are important to clarify the underlying mechanisms between FV intakes and sleep.

3.5.1 Strengths and limitations

In interpreting the results of our analyses, certain limitations of the study should be considered. Dietary intakes were collected at one time point only, which means any changes in dietary pattern over time were not taken into account. Self-report of FV

intakes in the UKWCS are above the national average (51), possibly due to over-reporting through the FFQ (52), which was observed in other cohort studies using this dietary assessment method (53). The method to assess sleep duration has not been validated, and self-reported sleep duration may cause over-reporting (54), and any change in sleep patterns were not taken into account. In addition, it was difficult to exclude the effects of other dietary polyphenols from other sources such as caffeine, red wine, and tea (55). Whilst inverse associations between FV intakes and sleep duration have been observed, effect size was small, and may not be clinically significant. Interpretation of the extent of causality should be undertaken with caution, since observational studies have substantial potential for biases caused by incomplete adjustments for confounders, measurement error in the exposure estimate, and biases in participation selection. On the other hand, our analyses have several strengths. The UKWCS is a large prospective cohort which includes health-conscious women with wide diversity in dietary intakes, which facilitates clarifying the associations between FV intakes and sleep duration. Furthermore, to our knowledge, this is the first study that has extensively investigated the associations between FV items and their polyphenol content on sleep duration in UK women using a validated dietary assessment tool. The use of Phenol Explorer as a reference database for polyphenol content has several advantages due to the high quality literature articles on polyphenol composition, the impacts of food processing on the polyphenols, and metabolite composition in the body. These advantages ensure that the polyphenol content of FV applied here were sensible with regard to the variety of polyphenols in each FV item.

3.6 Conclusions

FV intakes and their polyphenol content were associated with shorter sleep in a sub-group of UK women. Further investigations are required to assess the relationship between FV intakes and sleep measures in the general population using objective methods of sleep. Overall, the findings of this study do not provide strong evidence to suggest that polyphenol classes from FV intakes are important in relation to sleep duration. Until further knowledge is obtained from intervention studies, consumption of five or more servings/day of FV and sleeping 7–9 h/day for adults is recommended.

References of Chapter 3

1. Stranges S, Dorn JM, Cappuccio FP, et al. A population-based study of reduced sleep duration and hypertension: the strongest association may be in premenopausal women. *Journal of Hypertension*, 2010, **28**(5), pp.896-902.

2. Chaput JP, Despres JP, Bouchard C, et al. Association of sleep duration with type 2 diabetes and impaired glucose tolerance. *Diabetologia*, 2007, **50**(11), pp.2298-304.

3. Cappuccio FP, Cooper D, D'elia L, et al. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *European Heart Journal*, 2011, **32**(12), pp.1484-92.

4. Cappuccio FP, D'elia L, Strazzullo P, et al. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. *Sleep*, 2010, **33**(5), pp.585-92.

5. Yin J, Jin X, Shan Z, et al. Relationship of Sleep Duration With All-Cause Mortality and Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies. *Journal of the American Heart Association*, 2017, **6**(9).

6. St-Onge MP. Sleep-obesity relation: underlying mechanisms and consequences for treatment. *Obesity Reviews*, 2017, **18 Suppl 1**, pp.34-39.

7. Wu Y, Zhai L and Zhang D. Sleep duration and obesity among adults: a meta-analysis of prospective studies. *Sleep Medicine*, 2014, **15**(12), pp.1456-62.

8. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies. *International Journal of Epidemiology*, 2017, **46**(3), pp.1029-1056.

9. Noorwali EA, Cade JE, Burley VJ, et al. The relationship between sleep duration and fruit/vegetable intakes in UK adults: a cross-sectional study from the National Diet and Nutrition Survey. *Bmj Open*, 2018, **8**(4), p.e020810.

10. Peuhkuri K, Sihvola N and Korpela R. Diet promotes sleep duration and quality. *Nutrition Research*, 2012, **32**(5), pp.309-19.

11. Frank S, Gonzalez K, Lee-Ang L, et al. Diet and Sleep Physiology: Public Health and Clinical Implications. *Frontiers in Neurology*, 2017, **8**, p.393.

12. St-Onge M-P, Crawford A and Aggarwal B. Plant-Based Diets: Reducing Cardiovascular Risk by Improving Sleep Quality? *Current Sleep Medicine Reports*, 2018, **4**(1), pp.74-78.

13. Pifferi F, Dal-Pan A, Menaker M, et al. Resveratrol dietary supplementation shortens the free-running circadian period and decreases body temperature in a prosimian primate. *Journal of Biological Rhythms*, 2011, **26**(3), pp.271-5.

14. Pifferi F, Rahman A, Languille S, et al. Effects of dietary resveratrol on the sleep-wake cycle in the non-human primate gray mouse lemur (Microcebus murinus). *Chronobiology International*, 2012, **29**(3), pp.261-70.

15. Lin H, Tsai P, Fang S, et al. Effect of kiwifruit consumption on sleep quality in adults with sleep problems. *Asia Pacific Journal of Clinical Nutrition*, 2011, **20**(2), pp.169-74.

16. Pigeon W, Carr M, Gorman C, et al. Effects of a Tart Cherry Juice Beverage on the Sleep of Older Adults with Insomnia: A Pilot Study. *Journal of Medicinal Food*, 2010, **13**(3), pp.579-583.

17. Garrido M, Paredes SD, Cubero J, et al. Jerte Valley cherry-enriched diets improve nocturnal rest and increase 6-sulfatoxymelatonin and total antioxidant capacity in the urine of middle-aged and elderly humans. *The Journals of Gerontology.Series A, Biological Sciences and Medical Sciences*, 2010, **65**(9), pp.909-14.

18. Cade JE, Burley VJ, Alwan NA, et al. Cohort Profile: The UK Women's Cohort Study (UKWCS). *International Journal of Epidemiology*, 2017, **46**(2), p.e11.

19. Office for National Statistics. *The National Statistics Socio-economic classification (NS-SEC)* [online]. [Accessed 19 June 2017]. Available from: https://www.ons.gov.uk/methodology/classificationsandstandards/otherclassifications/thenationalstatisticssocioeconomicclassificationnssecrebasedonsoc2010.

20. Riboli E and Kaaks R. The EPIC project: Rationale and study design. *International Journal of Epidemiology*, 1997, **26**, pp.S6-S14.

21. Cade JE, Burley VJ, Greenwood DC, et al. The UK Women's Cohort Study: comparison of vegetarians, fish-eaters and meat-eaters. *Public Health Nutrition*, 2004, **7**(7), pp.871-878.

22. Cade JE, Burley VJ and Greenwood DC. Dietary fibre and risk of breast cancer in the UK Women's Cohort Study. *International Journal of Epidemiology*, 2007, **36**(2), pp.431-8.

23. Agency FS. *Food portion sizes* London, UK The stationary office, 2002.

24. Neveu V, Perez-Jimenez J, Vos F, et al. Phenol-Explorer: an online comprehensive database on polyphenol contents in foods. *Database: The Journal of Biological Databases and Curation*, 2010, **2010**, p.bap024.

25. Miranda AM, Steluti J, Fisberg RM, et al. Dietary intake and food contributors of polyphenols in adults and elderly adults of Sao Paulo: a population-based. *British Journal of Nutrition*, 2016, **115**(6), pp.1061-1070.

26. Miranda AM, Steluti J, Fisberg RM, et al. Association between Polyphenol Intake and Hypertension in Adults and Older Adults: A Population-Based Study in Brazil. *PloS One*, 2016, **11**(10), p.e0165791.

27. Lefevre-Arbogast S, Gaudout D, Bensalem J, et al. Pattern of polyphenol intake and the long-term risk of dementia in older persons. *Neurology*, 2018, **90**(22), pp.e1979-e1988.

28. Cleveland WS. Robust Locally Weighted Regression and Smoothing Scatterplots. *Journal of the American Statistical Association*, 1979, **74**(368), pp.829-836.

29. Cheynier V. Polyphenols in foods are more complex than often thought. *American Journal of Clinical Nutrition*, 2005, **81**(1), pp.223s-229s.

30. Stata Statistical Software: Release 15; StataCorp LLC: College Station, TX, USA, 2017.

31. Romain C, Alcaraz PE, Chung LH, et al. Regular consumption of HolisFiit, a polyphenol-rich extract-based food supplement, improves mind and body well-being of overweight and slightly obese volunteers: a randomized, double-blind, parallel trial. *International Journal of Food Sciences and Nutrition*, 2017, **68**(7), pp.840-848.

32. Manach C, Williamson G, Morand C, et al. Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies. *American Journal of Clinical Nutrition*, 2005, **81**(1 Suppl), pp.230S-242S.

33. Martin K and Appel C. Polyphenols as dietary supplements: A double-edged sword. *Nutrition & Dietetics*, 2009.

34. Ribas-Latre A, Del Bas JM, Baselga-Escudero L, et al. Dietary proanthocyanidins modulate melatonin levels in plasma and the expression pattern of clock genes in the hypothalamus of rats. *Molecular Nutrition & Food Research*, 2015, **59**(5), pp.865-78.

35. Gadacha W, Ben-Attia M, Bonnefont-Rousselot D, et al. Resveratrol opposite effects on rat tissue lipoperoxidation: pro-oxidant during day-time and antioxidant at night. *Redox Report:communications in free radical research*, 2009, **14**(4), pp.154-8.

36. Ribas-Latre A, Baselga-Escudero L, Casanova E, et al. Dietary proanthocyanidins modulate BMAL1 acetylation, Nampt expression and NAD levels in rat liver. *Scientific Reports*, 2015, **5**, p.10954.

37. Colwell CS. Rhythmic coupling among cells in the suprachiasmatic nucleus. *Journal of Neurobiology*, 2000, **43**(4), pp.379–388.

38. Potter GD, Cade JE, Grant PJ, et al. Nutrition and the circadian system. *Brtish Journal of Nutrition*, 2016, **116**(3), pp.434-42.

39. Mattson MP. Hormesis Defined. *Ageing Research reviews*, 2008, **7**(1), pp.1-7.

40. Ramis MR, Esteban S, Miralles A, et al. Caloric restriction, resveratrol and melatonin: Role of SIRT1 and implications for aging and related-diseases. *Mechanisms of Ageing and Development*, 2015, **146-148**, pp.28-41.

41. Lagouge M, Argmann C, Gerhart-Hines Z, et al. Resveratrol improves mitochondrial function and protects against metabolic disease by activating SIRT1 and PGC-1alpha. *Cell*, 2006, **127**(6), pp.1109-22.

42. Asher G, Gatfield D, Stratmann M, et al. SIRT1 regulates circadian clock gene expression through PER2 deacetylation. *Cell*, 2008, **134**(2), pp.317–328.

43. Orozco-Solis R, Ramadori G, Coppari R, et al. SIRT1 relays nutritional inputs to the circadian clock through the sf1 neurons of the ventromedial hypothalamus. *Endocrinology*, 2015, **156**(6), pp.2174–2184.

44. Mayer EA, Tillisch K and Gupta A. Gut/brain axis and the microbiota. *Journal of Clinical Investigation*, 2015, **125**(3), pp.926-38.

45. Leone V, Gibbons SM, Martinez K, et al. Effects of Diurnal Variation of Gut Microbes and High-Fat Feeding on Host Circadian Clock Function and Metabolism. *Cell Host & Microbe*, 2015, **17**(5), pp.681-689.

46. Liang X, Bushman FD and Fitzgerald GA. Rhythmicity of the intestinal microbiota is regulated by gender and the host circadian clock. *Proceedings of the National Academy of Sciences of the United States of America*, 2015, **112**(33), pp.10479-10484.

47. Blade C, Aragones G, Arola-Arnal A, et al. Proanthocyanidins in health and disease. *Biofactors*, 2016, **42**(1), pp.5-12.

48. Selma MVE, J.C.; Tomás-Barberán, F.A. Interaction between phenolics and gut microbiota: Role in human health. *Journal of Agricultural and Food Chemistry*, 2009, **57**(15), pp.6485–6501.

49. Margalef MG, L.; Pons, Z.; Bravo, F.I.; Arola, L.; Muguerza, B.; Arola-Arnal, A. A. A dose–response study of the bioavailability of grape seed proanthocyanidin in rat and lipid-lowering effects of generated metabolites in HepG2 cells. *Food Research International (Ottawa, Ont.)*, 2014, pp.500–507.

50. Wagnerova A, Babickova J, Liptak R, et al. Sex Differences in the Effect of Resveratrol on DSS-Induced Colitis in Mice. *Gastroenterology Research and Practice*, 2017, **2017**, p.8051870.

51. Whitton C, Nicholson SK, Roberts C, et al. National Diet and Nutrition Survey: UK food consumption and nutrient intakes from the first year of the rolling programme and comparisons with previous surveys. *British Journal of Nutrition*, 2011, **106**(12), pp.1899-1914.

52. Cade JE, Burley VJ, Warm DL, et al. Food-frequency questionnaires: a review of their design, validation and utilisation. *Nutrition Research Reviews*, 2004, **17**(1), pp.5-22.

53. Brunner E, Stallone D, Juneja M, et al. Dietary assessment in Whitehall II: comparison of 7 d diet diary and food-frequency questionnaire and validity against biomarkers. *The British Journal of Nutrition*, 2001, **86**(3), pp.405-14.

54. Lauderdale DS, Knutson KL, Yan LL, et al. Self-reported and measured sleep duration: how similar are they? *Epidemiology*, 2008, **19**(6), pp.838-45.

55. Perez-Jimenez J, Neveu V, Vos F, et al. Identification of the 100 richest dietary sources of polyphenols: an application of the Phenol-Explorer database. *European Journal of Clinical Nutrition*, 2010, **64 Suppl 3**, pp.S112-20.

Chapter 4: The relationship between sleep duration and fruit/vegetable intakes in UK adults: a cross-sectional study from the National Diet and Nutrition Survey

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4.1 Abstract

Objectives: There is increasing evidence to suggest an association between sleep and diet. The aim of the present study was to examine the association between sleep duration and FV intakes and their associated biomarkers in UK adults.

Design: Cross-sectional.

Setting: Data from the National Diet and Nutrition Survey.

Participants: 1612 adults aged 19-65 years were included, pregnant/breastfeeding women were excluded from the analyses.

Outcome measures: Sleep duration was assessed by self-report, and diet was assessed by 4-day food diaries, disaggregation of foods containing FV into their components was conducted to determine total FV intakes. Sleep duration was divided into: short (<7 hours/day), reference (7–8 hours/day) and long (>8 hours/day) sleep periods. Multiple regression adjusting for confounders was used for analyses where sleep duration was the exposure and FV intakes and their associated biomarkers were the outcomes. Restricted cubic spline models were developed to explore potential non-linear associations.

Results: In adjusted models, long sleepers (LS) consumed on average 28 (95% CI −50 to −6, p = 0.01) g/day less of total FV compared to reference sleepers (RS), whereas short sleepers (SS) consumed 24 g/ day less (95% CI −42 to –6, p = 0.006) and had lower levels of FV biomarkers (total carotenoids, β-carotene and lycopene) compared to RS. Restricted cubic spline models showed that the association between sleep duration and FV intakes was non-linear (p<0.001) with RS having the highest intakes compared to SS and LS. The associations between sleep duration and plasma total carotenoids (p = 0.0035), plasma vitamin C (p = 0.009) and lycopene (p<0.001) were non-linear with RS having the highest levels.

Conclusions: These findings show a link between sleep duration and FV consumption. This may have important implications for lifestyle and behavioural change policy.

4.2 Introduction

The consumption of FV has shown to improve overall health (1) and reduce the risk of chronic diseases (2-4) when 400 grams or more are consumed as recommended by WHO (5). Hence, identifying lifestyle factors associated with higher intakes of FV is a public health priority. The relationship between sleep duration and risk of obesity was reported in a recent meta-analysis with short sleep duration associated with a 45% increased risk of obesity due to several behavioural mechanisms including the reduced intake of FV (6). Thus, it is essential to study FV consumption in relation to sleep duration. There are limited studies assessing the association between sleep duration and FV consumption in UK adults using validated and detailed dietary data (7). To our knowledge, this study is the first to use data that disaggregated foods containing FV into their components which helped in assessing total FV intake. Therefore, this study aims to assess the relationship between sleep duration and daily FV consumption and their associated biomarkers in adults aged 19-65 years using data of the NDNS (years 1-4) that represent the UK population.

4.3 Methods

4.3.1 Study population

The NDNS is a government-commissioned rolling programme that started in 1992 to assess diet, nutrient intake and nutritional status of the UK population (8). This study used combined data from years 1-4 of the rolling programme (2008/2009–2011/2012) for adults aged 19-65 years (9). Between April 2008 and March 2011, random samples of 21,573 addresses from 799 postcode sectors were drawn from the UK Postcode Address File. Households were selected randomly and within the household either one adult (aged 19 years and over) and one child (aged 1.5-18 years), or one child were randomly selected to participate (8).

4.3.2 Dietary records

The NDNS assessed dietary intake using a 4-day estimated diary that included instructions on how to complete the diary, as described in detail elsewhere (8). Participants were asked to record food and drinks consumed both at home and away from home for four consecutive days. Participants were asked to record portion sizes as instructed or in household measures. They were asked to record brand names, ingredients and quantities, cooking methods, leftovers and dietary supplements. Dietary intake was calculated by trained coders and editors in the Diet In Nutrients Out dietary

assessment system which calculates food and beverage nutrient intake based on data for >6000 foods. Detailed information on data coding is provided elsewhere (8).

4.3.3 Fruit and vegetable intake

To determine the total intakes of FV, disaggregation of foods containing FV into their components was conducted by NDNS. FV content of soft drinks, confectionery, cakes (including fruit cake) and biscuits, sugar preserves (including jam) and sweet spreads, savoury snacks and ice cream were excluded from the estimates because they fell into the high fat/high sugars segment of the eat well plate (10). The disaggregation process and the calculation of five-a-day portions using disaggregated data is described elsewhere (8, 11).

4.3.4 Blood sampling (FV biomarkers)

Samples were collected between February 2008 and July 2012; years 1-4 of the NDNS Rolling Programme. In year 1, there was a 2-week time lag between the start of the interviewer and nurse stages. From year 2 onwards, the gap was extended, to an average of 8 weeks, with the aim of increasing nurse stage response rates. Participants were asked a series of screening questions prior to venepuncture to assess their eligibility for giving a blood sample. Participants with a bleeding or clotting disorder or those taking anticoagulant medications were excluded from providing a blood sample. The blood taking procedures including collection, processing, analysing and quality control of the blood samples are explained in further detail elsewhere (8). This study considered available biomarker measurements related to FV consumption namely plasma vitamin C, total carotenoids, α-carotene, β-carotene and lycopene. The detailed procedure for vitamin C and carotenoid analyses is described elsewhere (8).

4.3.5 Sleep duration

Participants were asked about sleep duration in the following form for week nights and weekends by using a computer-assisted personal interview programme:

“Over the last seven days, that is since (date) how long did you usually sleep for on weeknights, that is, Sunday to Thursday nights?”

“And over the last seven days, how long did you usually sleep for on a weekend that is Friday and Saturday nights?”

An average time per night was sought and if respondents worked on night shifts during the last 2 weeks/weekends, the average time slept during the day should be entered.

For this study, two separate variables were generated for sleep duration based on weekdays and weekends for all adults aged 19-65 years from years 1-4 in NDNS. Average sleep duration for weekdays and weekends was calculated using the following equation ((minutes slept during the week×5) + (minutes slept during weekends×2))/7. Sleep duration was categorised based on the literature (12-14) to short sleepers (SS) (<7 hours (420 minutes)), reference sleepers (RS) (7-8 hours (≥420 minutes and ≤480 minutes)) and long sleepers (LS) (>8 hours (>480 minutes)).

4.3.6 Statistical analyses

Descriptive statistics such as means and proportions were conducted to describe adults from the NDNS according to sleep duration categories. P values of <0.05 represent statistical significance. Multiple regression analyses was used to assess the relationship between sleep duration, FV intakes and biomarkers. Model 1 included adjustment for age and sex only whereas model 2 was adjusted for potential confounders that were identified after the development of a directed acyclic graph these were age, sex, SES assessed by NS-SEC including eight categories (15), smoking status (16-19) (current, ex-smoker and never), ethnicity (white, non-white) and energy intake from food. In all analyses, sleep duration was used as the exposure and FV intakes and biomarkers were the outcomes.

We used restricted cubic splines to model non-linear relationships between sleep duration as a continuous exposure (hour/day) and total FV intakes as the outcomes (grams/day). The splines comprised two polynomial segments separated by three knots (at the following percentiles of sleep duration 10, 50 and 90 as recommended by Harrell (20)) with linear regions before the first knot and after the last.

Sensitivity analyses were conducted including: 1) considering weekdays and weekends separately; and separate analyses were conducted after 2) excluding participants who consumed vitamins, minerals or/and supplements in the previous year (526 participants); 3) excluding those who self-reported currently having a long-standing illness (Appendix D (D.8.) for illnesses included) (547 participants); 4) excluding those taking prescribed medicines (566 participants) 5) excluding those who reported being vegetarian (39 participants) 6) including BMI and physical activity as an additional adjustment to the potential confounders in model 2 and 7) stratifying the analyses between sleep duration and FV intakes by BMI. Statistical analyses were conducted using IC Stata V.13 (21), missing data were automatically dropped.

4.4 Results

General characteristics of NDNS adult participants aged 19-65 years according to sleep duration category are shown in Table 4.1. Eighty participants were excluded from the analyses due to lack of sleep data or pregnancy/breast feeding (Figure 4.1.). The 1612 adults included in the study had a mean age of 43 years (95% CI 43 to 44) and a mean BMI of 25 kg/m2 (95% CI 25 to 26). Thirty-three per cent (n=539) of the participants were SS, 49% of the participants (n=788) were RS and 18% (n=285) of the participants were LS. In total, 57% (95% CI 55% to 60%) of the participants were female, 90% (95% CI 89% to 92%) were white, 46% (95% CI 43% to 49%) reported taking prescribed medicines and 54% (95% CI 52% to 57%) never smoked.

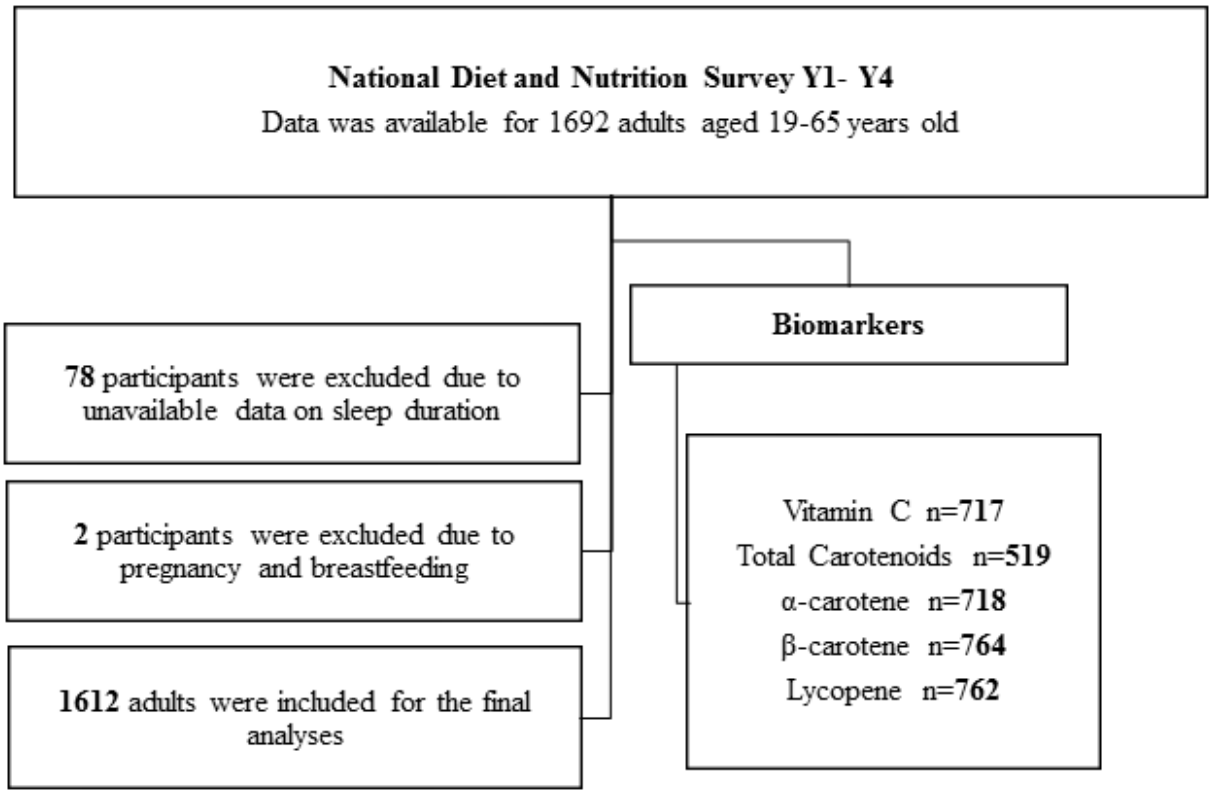

Figure 4.1. Participants flow chart.

Table 4.1. Participant characteristics according to sleep duration category.

Characteristics	Sleep Categories <7 hours/day (SS)	7-8 hours/day (RS)	> 8 hours/day (LS)	Total
Observations (n)	539	788	285	1612
	Mean (95%CI)	**Mean (95%CI)**	**Mean (95%CI)**	**Mean (95%CI)**
Age (Years)	45 (44, 46)	44 (43, 45)	39 (38 ,40)	43 (43,44)
BMI	26 (25,27)	25 (25,26)	24 (23, 25)	25 (25,26)
Food energy	1712 (1665, 1758)	1769 (1731,1807)	1645 (1587,1703)	1727 (1701,1752)
Equivalised household income	33K (31K, 35K)	34K (32K, 36K)	29K (26K,32K)	33K (32K, 34K)
Fruit (g/d)	98 (89, 106)	115 (107, 124)	82 (73, 92)	103 (98, 108)
Vegetables (g/d)	178 (168, 188)	194 (187, 201)	168 (157, 180)	185 (180, 190)
Total FV (g/d)	276 (261, 291)	309 (297, 322)	250 (233, 267)	287 (279, 296)
Plasma vitamin C (µmol/l)	48 (45, 51)	53 (51, 55)	56 (53, 59)	51 (50, 53)
Plasma total carotenoids (µmol/l)	2.2 (2.1, 2.4)	2.5 (2.4, 2.7)	2.4 (2.2 ,2.7)	2.4 (2.3, 2.5)
Plasma Lycopene (µmol/l)	0.62 (0.57, 0.67)	0.73 (0.69 , 0.77)	0.69 (0.61,0.76)	0.69 (0.66 , 0.72)
	% (95%CI)	**% (95%CI)**	**% (95%CI)**	**% (95%CI)**
Sex (Female)	55 (51, 59)	56 (52, 59)	64 (58, 69)	57 (55, 60)
Ethnicity (White)	92 (90, 94)	89 (86, 91)	88 (84, 91)	90 (89, 92)
Has longstanding illness (Yes)	37 (33, 41)	30 (26, 32)	39 (33, 45)	34 (32, 36)
Taking prescribed medicine (Yes)	47 (42, 51)	43 (38, 46)	53 (46, 60)	46 (43,49)
Employer (Full or part-time employment)	68 (64, 72)	72 (68, 75)	62 (56, 67)	69 (67,71)
SES (Lower managerial and professional)	28 (24,32)	28 (25,31)	22 (17,27)	27 (24,29)
Smoking (Never)	51 (46,55)	57 (53, 60)	54 (48, 60)	54 (52,57)
Consuming 5 or more portions of FV/day (Yes)	28 (24, 32)	35 (31, 38)	25 (21, 31)	31 (29, 33)
Vegetarian (Yes)	2 (1,3)	3 (2,4)	0.7 (0.1, 2)	2 (1,3)
Has one child aged between 0-4 years	15 (12, 18)	13 (10,15)	12 (8,16)	13 (12,15)
Frequency of drinking alcohol in past 12 months (once or twice a week or month)	45 (40, 49)	48 (44, 51)	50 (44, 55)	47 (45, 50)

Legend: BMI (body mass index), d (day), FV (fruits and vegetables), g (gram), LS (long sleepers), l (litre), µmol (micromole), n (number), RS (reference sleepers), SES (socioeconomic status), SS (short sleepers).

Concerning FV consumption, 35% (95% CI 31% to 38%) of RS consumed five or more portions/day of FV whereas 25% (95% CI 21% to 31%) of LS and 28% (95% CI 24% to 32%) of SS consumed five or more portions of FV/day. LS consumed a mean of 250 (95% CI 233 to 267) g/day of total FV, RS consumed a mean of 309 (95% CI 297 to 322) g/day of total FV whereas SS had a mean intake of 276 (95% CI 261 to 291) g/day of total FV (Table 4.1.).

In adjusted analyses (model 2) (Table 4.2.), SS and LS ate less fruit (g/day), FV portions and total FV (g/day) compared with RS. SS ate on average 13 g/day (95% CI −24 to –2, p = 0.01) less total fruit, 0.2 (95% CI −0.5 to –0.06, p = 0.01) less portions/day of FV and 24 g/day (95% CI −42 to –6, p=0.006) less total FV compared with RS. LS consumed on average 16 g/day (95% CI −30 to –2, p = 0.01) less total fruit, 0.2 (95% CI −0.5 to 0.01, p = 0.06) less portions/day of FV and 28 g/day (95% CI −50 to –6, p = 0.01) less total FV compared with RS. In model 1, SS had on average 17 g/ day (95% CI −29 to –5, p = 0.004) and LS had on average 19 g/day (95% CI −34 to –4, p = 0.009) less vegetable intake compared with RS, but the differences became borderline significant with further adjustment.

In adjusted analyses (model 2) (Table 4.2.), SS had lower levels of plasma FV biomarkers except α-carotene and vitamin C compared with RS. In contrast, LS had higher vitamin C levels compared with RS. LS had 4 μmol/L higher plasma vitamin C (95% CI 0.1 to 8, p = 0.04) compared with RS. SS had 0.2 μmol/L lower plasma total carotenoids (95% CI −0.4 to –0.08, p= 0.004), 0.05 μmol/L lower plasma β-carotene (95% CI −0.1 to –0.009, p = 0.01) and 0.08 μmol/L lower plasma lycopene (95% CI −0.1 to –0.02, p = 0.005) compared with RS. This was confirmed with SS having less intake of tomatoes compared with RS in adjusted models (−5 g/day, 95% CI −9 to –0.1, p = 0.04). SS had a mean intake of 42 g/day (95% CI 38 to 46) of tomatoes, RS had 48 g/day (95% CI 45 to 51) and LS had 41 g/day (95% CI 36 to 46).

Table 4.2. The association between sleep duration categories and FV consumption and their biomarkers.

Short sleepers (<7h/d) and Long sleepers (>8h/d) compared to the reference group (7-8 h/d)								
Models	**Model 1 (n=1612)**				**Model 2 (n= 1610)**			
	Short sleepers <7 hours/day		**Long sleepers >8 hours/day**		**Short sleepers <7 hours/day**		**Long sleepers >8 hours/day**	
FV intake	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**
Total fruit[a] (g/day)	-19 (-31, -8)	0.001	-24 (-38 ,-10)	0.001	-13 (-24, -2)	0.01	-16 (-30, -2)	0.01
Total veg[b] (g/day)	-17 (-29, -5)	0.004	-19 (-34 ,-4)	0.009	-10 (-21, 0.5)	0.06	-11 (-25, 2)	0.09
FV portions[c]	-0.4 (-0.6, -0.2)	<0.001	-0.5 (-0.8, -0.1)	0.001	-0.2 (-0.5, -0.05)	0.01	-0.2 (-0.5 ,-0.01)	0.04
5-a-day portions[d]	-0.4 (-0.7, -0.2)	<0.001	-0.5 (-0.8, -0.1)	0.002	-0.2 (-0.5, -0.06)	0.01	-0.2 (-0.5, 0.01)	0.06
Total FV[e](g/day)	-37 (-56, -18)	<0.001	-44 (-67, -20)	<0.001	-24 (-41, -6)	0.006	-28 (-50, -6)	0.01
Nutrients (mg/d)								
Vitamin C diet only	-9 (-16 , -2)	0.01	-10 (-19, -1)	0.02	-5 (-12, 1)	0.1	-4 (-12, 4)	0.3
Vitamin C *	-13 (-27, 0.8)	0.06	-21 (-39, -3)	0.01	-7 (-21, 6)	0.2	-12 (-30,5)	0.1
Biomarkers (µmol/l)								
Vitamin C	-4 (-8, -1)	0.006	3 (-1 , 7)	0.1	-2 (-6, 0.3)	0.07	4 (0.1, 8)	0.04
Total carot[f]	-0.2 (-0.4, -0.1)	0.002	-0.1 (-0.3, 0.1)	0.3	-0.2 (-0.4, -0.08)	0.004	-0.06 (-0.2 ,0.1)	0.5
α-carotene	-0.01 (-0.02,0.003)	0.1	-0.009 (-0.02 , 0.007)	0.2	-0.006 (-0.01, 0.007)	0.3	-0.004 (-0.02, 0.01)	0.6
β-carotene	-0.07 (-0.1, -.02)	0.003	-0.01 (-0.07 , 0.05)	0.7	-0.05 (-0.1 ,-0.009)	0.01	0.009 (-0.05, 0.07)	0.7
Lycopene	-0.1 (-0.1 ,-0.04)	0.001	-0.06 (-0.1 ,0.01)	0.09	-0.08 (-0.1, -0.02)	0.005	-0.05 (-0.1, 0.02)	0.1

Legend: FV (fruits and vegetables), G (gram), l (litre), mg (milligram), µmol (micromole), n (number), veg (vegetables).
Model 1 adjusted for age and sex
Model 2 adjusted for age, sex, socio-economic status, smoking, ethnicity and food energy

a) Total fruit (not including juice) = Fruit (g)+Dried fruit (g)+ Smoothie fruit (g)
b) Total vegetables= Beans (g) + Brassicaceae (g) + Other vegetables (g) + Tomatoes (g) + Tomato Puree (g) +Yellow Red Green (g)
c) FV portions= (Fruit (g) + Driedfruitx3_mean + Tompureex5 mean + beans max mean+ Brassicaceae (g) + Yellow Red Green (g) + Other vegetables (g) + Tomatoes (g))/ 80
d) 5-a-day portions(portions/day)= Fruit/vegetable portions + Fruit juice portions+ Smoothie fruit portions
e) Total FV (not including juice) = Total fruit +Total vegetables
f) Total carotenoids = Lutein + alpha-cryptoxanthin + beta-cryptoxanthin+ lycopene + alpha-carotene + beta-carotene *Vitamin C including supplements

Restricted cubic spline modelling (Figure 4.2.) showed that the association between sleep duration and total FV intake (g/day) was non-linear ($p < 0.001$) with participants sleeping 7–8 hours/day having the highest intakes compared with SS and LS. Similarly, the association between sleep duration and plasma biomarkers (Figure 4.3.) vitamin C ($p = 0.009$) (Figure 4.3.A.), total carotenoids ($p = 0.0035$) (Figure 4.3.B.) and lycopene ($p < 0.001$) (Figure 4.3.C.) were non-linear.

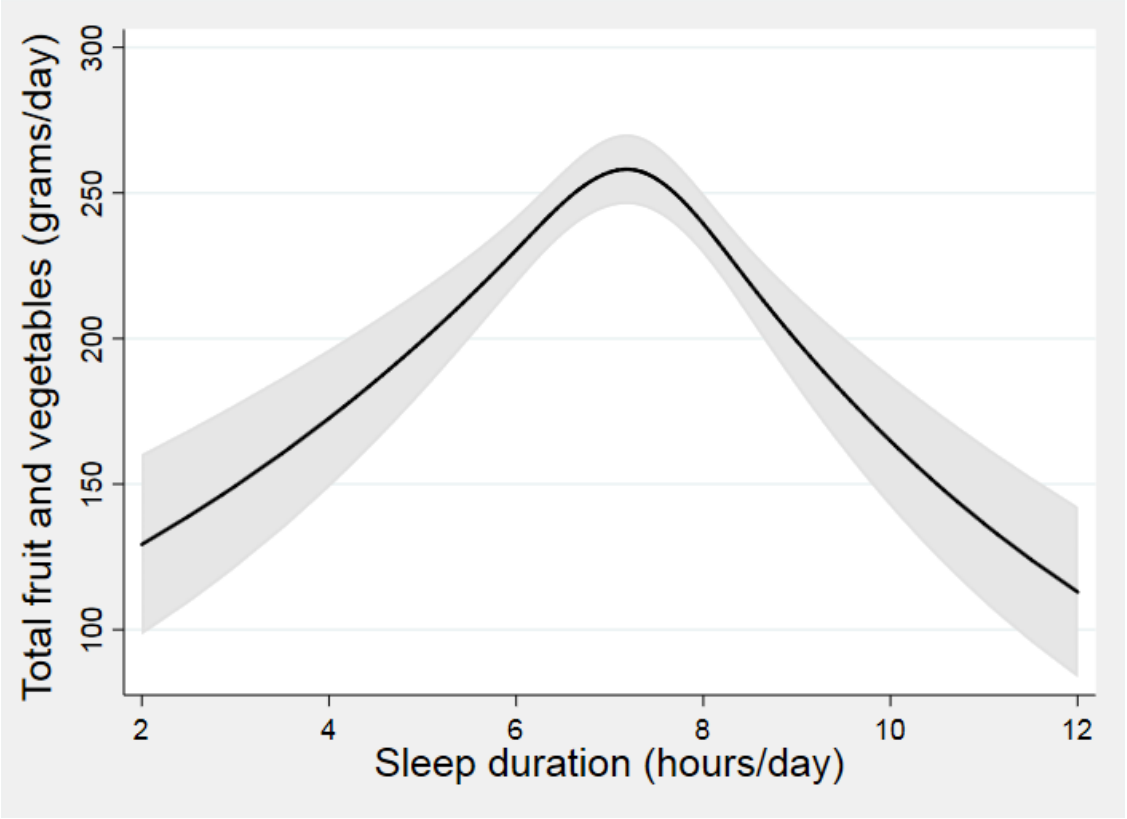

Figure 4.2. The association between sleep duration and FV consumption from the restricted cubic splines.

Black line plots the predicted FV intakes with 95% CI (grey-shaded area) for typical participants (females, white, non-smokers, and lower managerial and professional occupation).

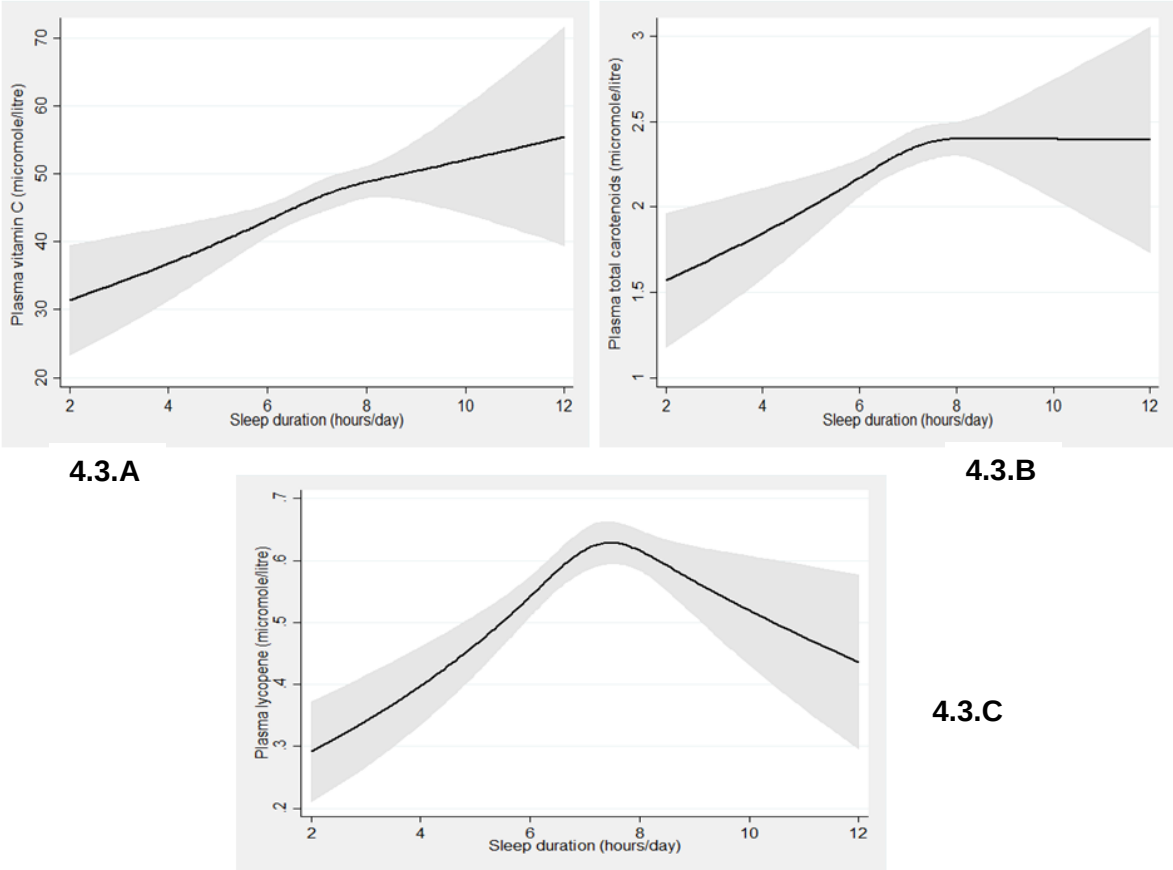

Figure 4.3. The association between sleep duration and FV biomarkers from the restricted cubic spline modelling.

Association between sleep duration and fruit/vegetable (FV) biomarkers from the restricted cubic spline modelling. Black lines plot the predicted FV biomarkers values: (4.3.A) vitamin C, (4.3.B) total carotenoids, (4.3.C) lycopene with 95% CI (grey-shaded area) for typical participants (females, white, non-smokers, lower managerial and professional occupation).

4.4.1 Sensitivity analyses

Sensitivity analysis showed broadly similar results (Appendix D (D.1.-D.7.)). Including adjustment for BMI and physical activity in the fully adjusted model did not affect the results. Results of separate analyses excluding participants who consumed minerals, vitamins and/or food supplements, being vegan/vegetarian, having a long-standing illness and consuming prescribed medicines, remained similar with SS consuming less FV in comparison to RS but no difference between LS FV intakes and RS. The associations between sleep duration and biomarkers were similar with SS having lower levels compared with RS and LS having higher levels of plasma vitamin C compared with RS. Results dividing the exposure into weekday and weekend sleep duration were similar, SS on average consumed less g/day of FV and had lower levels of biomarkers on weekdays and weekends compared with RS. LS on average consumed less g/day of FV on weekdays compared with RS.

4.5 Discussion

To our knowledge, this is the first nationally representative study to examine the association between sleep duration and FV intakes using disaggregated data among UK adults. The results of this study show SS and LS have lower intakes of FV compared with RS. Results of FV biomarkers show lower levels of all plasma biomarkers except α-carotene and vitamin C in SS compared with RS in contrast to plasma vitamin C levels in LS which were higher than RS. Similar results were noted after further adjustment for BMI and physical activity, excluding participants who had a long-standing illness, consumed prescribed medicines and those who consumed supplements, minerals or/and vitamins in the previous year. The associations between sleep duration, FV intake and biomarkers were non-linear with RS having the highest intakes and levels of biomarkers compared with SS and LS as shown in the restricted cubic spline modelling. Thus, these findings suggest that among UK adults RS have the highest intakes of FV compared with SS and LS.

These results are in line with several other cross-sectional studies (12, 13, 22-24). Although the studies differed in sample size, ethnicity, dietary assessment methods and categorisation of sleep duration, the results showed a lower intake of FV in SS/LS compared with RS. Women with short and long sleep durations had low intakes of FV in the USA or Puerto Rico (22) which was similar to the results of this study. Additionally, short sleep duration was associated with obesity-related behaviours including low FV consumption in rural communities in Missouri, Tennessee and Arkansas (23). In a study

that examined the association between sleep duration and diet quality among women following childbirth, short sleep duration was not associated with diet quality whereas long sleep duration was associated with lower consumption of total and whole fruit (25). Katagiri et al. (26) measured the association between sleep quality and diet and noted that poor sleep quality was significantly associated with low intakes of total vegetables, green/yellow vegetables and other vegetables. The study suggested that the relationship of dietary intake with sleep quality is similar to that with sleep duration.

Regarding the results of FV biomarkers, our results were supported by two other studies (12, 27). Grandner et al. (27) showed a significant lower intakes of lycopene in very SS (<5 hours). Beydoun et al. (12) reported that short sleep duration was associated with lower serum levels of vitamin C, total carotenoids, α-carotene and β-carotene compared with RS. It is unclear why the results of this study observed a higher plasma vitamin C levels in LS, however, this may be explained by differences in food variety or misreporting of diet intake (27). This also could be due to biomarkers measuring long-term dietary intake while diet intake was assessed by a 4-day food diary.

In contrast, a recent study examined the association between sleep duration and cardiovascular risk behaviours using data from the UK biobank found results which were inconsistent with our own. Long sleep duration was positively associated with vegetable intake (28). These results which contrast with our findings may be due to the different assessment methods of sleep duration and FV intake. Sleep duration assessment in the UK biobank did not consider weekday and weekend sleep duration separately as conducted in the NDNS study since sleep duration may differ between those days (29). Furthermore, self-report of sleep duration may differ by question format by reporting short sleep duration when asked a single question (30). Sleep duration in the UK biobank study was assessed by asking one question in regard to sleep every 24 hours whereas our study assessed sleep duration by asking two separate questions of sleep based on weeknights and weekends. FV intakes were assessed differently in the UK biobank (28) and the NDNS (11).

Patterson et al. (28) assessed FV intake by considering diet intake in the previous year and asking how many pieces of fresh fruit would participants eat per day and how many heaped table-spoons of vegetables participants would eat on average per day. This method was based on the UK guidelines that a portion of vegetables is three heaped tablespoons whereas the NDNS assessed dietary intake using a 4-day estimated diary and disaggregated foods containing FV which is considered a better estimate of average

intakes compared with other dietary assessment methods (31). Additionally, this study conducted supportive biomarker analyses. In a home-based intervention study that assessed the effects of extended bedtimes on sleep duration and food desire, desire for FV was not affected by added sleep (32). However, the study had several limitations including a small sample size which may limit the generalisability to more diverse populations. One of the major limits of the intervention study (32) is the short duration of intervention (2 weeks) which does not measure the potential effects over a longer period. Experimental studies differ from free-living individuals; therefore, it is required to consider the potential for non-representative samples taking part in experimental studies. Furthermore, the association between FV intake and sleep duration was assessed among American pregnant women. Total daily FV consumption was not associated with sleep duration (33). This could be due to the different sample and dietary assessment methods. FV was assessed by asking women how many times per day, week or month they consumed FV.

Several potential mechanisms may underlie the association between sleep duration and diet intake (7, 34, 35). Short sleep duration or disrupted sleep may lead to emotional stress, impaired decision-making, and increased reward sensitivity to calorie-dense foods and lower FV intake. Changes in appetite hormones, ghrelin and leptin, due to lack/disrupted sleep may increase the preference for energy-dense foods leading to lower intakes of FV. Although potential mechanisms were not measured in this study, they may be the underlying reasons for decreased intake of FV in SS and LS. On the other hand, sleep may be promoted by foods such as kiwifruits, tart cherries, milk, and chamomile tea for their impact on tryptophan availability and the synthesis of serotonin and melatonin (36). This provides insight to the relationship between sleep and diet being potentially reciprocal. Future interventional trials are required to incorporate objective measures of sleep to clarify the relationships between sleep and FV intakes. Sleep extension intervention has been reported to reduce the intakes of free sugars in a 4-week randomised controlled pilot trial (37). Longer term, fully powered sleep extension studies on FV intake and their associated biomarkers are needed to confirm these results.

4.5.1 Strengths and limitations of the study

The main strength of this study was the disaggregation of foods containing FV into their components which helped in assessing total FV intake (11). Furthermore, the 4-day estimated diary has been validated against several biomarkers and demonstrated better

estimates of average intakes compared with other dietary assessment methods. This study has several limitations including the self-report of sleep duration which was based on memory and could cause over-reporting (38). Further limitations include lack of consideration of other sleep factors such as sleep quality (26), sleep timing (39), sleep problems, typical week information, shift-work, and chronotype (28). In year 1, weekend days were oversampled and in year 2, they were under sampled to redress that however, in the years 1-4 combined data there still remains a slightly higher proportion of weekend days. Eating habits vary between weekdays and weekends (40) which could lead to a bias in the reporting of FV intake. The small number of participants in the obtained biomarkers was a further limitation. The association between sleep duration and FV intake is a reciprocal relationship and the causal pathways underlying the relationship cannot be detected in cross-sectional studies (26).

4.5.2 Public health implications

Sleep duration among UK adults has been declining recently with 70% of UK adults sleeping less than 7 hours/night according to the Sleep Council (41). Additionally, the intake of FV is decreasing among UK adults with only 30% of them meeting the 5-a-day recommendation according to the NDNS results provided by Public Health England (8). If the results of this study were confirmed in prospective and interventional studies this would highlight the importance of translating the scientific evidence focusing on the relationship between sleep and diet into practical messages that can help the public to prevent chronic diseases. This would include making different populations aware of the relationship between sleep and diet by providing more information on sleep in national dietary guidelines to enhance healthy lifestyle recommendations. In addition, this information can be incorporated in hospitals to educate healthcare professionals, weight-loss programmes and other programmes targeting improvement in overall health. This information is also essential for those caring for at risk groups such as the elderly and those with chronic diseases (42).

4.6 Conclusions

The results of this study suggest a link between sleep duration and FV intake. Sleep duration was non-linearly related to self-reported FV intakes and their associated biomarkers with RS having the highest intakes of FV and levels of associated biomarkers compared with SS and LS. These results may have important implications for lifestyle and behavioural change policy.

References of Chapter 4

1. Wang X, Ouyang YY, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. *Bmj-British Medical Journal*, 2014, **349**.

2. Ishihara J, Umesawa M, Okada C, et al. *Reference module in biomedical sciences.* Elsevier. 2014.

3. Liu S, Manson JE, Lee IM, et al. Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study. *American Journal of Clinical Nutrition*, 2000, **72**(4), pp.922-928.

4. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies. *International Journal of Epidemiology*, 2017, **46**(3), pp.1029-1056.

5. WHO. *Diet, nutrition and the prevention of chronic diseases* [online]. 2003. [Accessed 6 November 2015]. Available from: http://apps.who.int/iris/bitstream/handle/10665/42665/WHO_TRS_916.pdf?sequence=1.

6. Wu Y, Zhai L and Zhang D. Sleep duration and obesity among adults: a meta-analysis of prospective studies. *Sleep Medicine*, 2014, **15**(12), pp.1456-62.

7. Dashti HS, Scheer FA, Jacques PF, et al. Short sleep duration and dietary intake: epidemiologic evidence, mechanisms, and health implications. *Advances in Nutrition*, 2015, **6**(6), pp.648-59.

8. Bates B, Lennox A, Prentice A, et al. *National Diet and Nutrition Survey Results from years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009-2011/2012).* [online]. 2014. [Accessed 18 January 2016]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/594361/NDNS_Y1_to_4_UK_report_full_text_revised_February_2017.pdf.

9. UK Data Service. *National Diet and Nutrition Survey Years 1-4* [online]. 2015. [Accessed 20 January 2016]. Available from: https://beta.ukdataservice.ac.uk/datacatalogue/doi/?id=6533.

10. NHS. *The Eatwell Guide* [online]. 2019. [Accessed 7 October 2016]. Available from: https://www.nhs.uk/live-well/eat-well/the-eatwell-guide/.

11. Fitt E, Mak TN, Stephen AM, et al. Disaggregating composite food codes in the UK National Diet and Nutrition Survey food composition databank. *European Journal of Clinical Nutrition*, 2010, **64 Suppl 3**, pp.S32-6.

12. Beydoun MA, Gamaldo AA, Canas JA, et al. Serum nutritional biomarkers and their associations with sleep among US adults in recent national surveys. *PloS One*, 2014, **9**(8), p.e103490.

13. Haghighatdoost F, Karimi G, Esmaillzadeh A, et al. Sleep deprivation is associated with lower diet quality indices and higher rate of general and central obesity among young female students in Iran. *Nutrition*, 2012, **28**(11-12), pp.1146-50.

14. Cassidy S, Chau JY, Catt M, et al. Cross-sectional study of diet, physical activity, television viewing and sleep duration in 233,110 adults from the UK Biobank; the behavioural phenotype of cardiovascular disease and type 2 diabetes. *BMJ Open*, 2016, **6**(3), p.e010038.

15. Office for National Statistics. *The National Statistics Socio-economic classification (NS-SEC)* [online]. [Accessed 27 March 2016]. Available from: https://www.ons.gov.uk/methodology/classificationsandstandards/otherclassifications/thenationalstatisticssocioeconomicclassificationnssecrebasedonsoc2010.

16. Zhang L, Samet J, Caffo B, et al. Cigarette smoking and nocturnal sleep architecture. *American Journal of Epidemiology*, 2006, **164**(6), pp.529-37.

17. Jaehne A, Unbehaun T, Feige B, et al. How smoking affects sleep: a polysomnographical analysis. *Sleep Medicine*, 2012, **13**(10), pp.1286-92.

18. Lohse T, Rohrmann S, Bopp M, et al. Heavy Smoking Is More Strongly Associated with General Unhealthy Lifestyle than Obesity and Underweight. *PloS One*, 2016, **11**(2).

19. Palaniappan U, Starkey LJ, O'loughlin J, et al. Fruit and vegetable consumption is lower and saturated fat intake is higher among Canadians reporting smoking. *Journal of Nutrition*, 2001, **131**(7), pp.1952-1958.

20. Harrell F. *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis.* New York Springer, 2001.

21. StataCorp. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP, 2013.

22. Kim S, Deroo LA and Sandler DP. Eating patterns and nutritional characteristics associated with sleep duration. *Public Health Nutrition*, 2011, **14**(5), pp.889-95.

23. Stamatakis KA and Brownson RC. Sleep duration and obesity-related risk factors in the rural Midwest. *Preventive Medicine*, 2008, **46**(5), pp.439-44.

24. Mossavar-Rahmani Y, Jung M, Patel SR, et al. Eating behavior by sleep duration in the Hispanic Community Health Study/Study of Latinos. *Appetite*, 2015, **95**, pp.275-84.

25. Xiao RS, Moore Simas TA, Pagoto SL, et al. Sleep Duration and Diet Quality Among Women Within 5 Years of Childbirth in the United States: A Cross-Sectional Study. *Maternernal and Child Health Journal*, 2016, **20**(9), pp.1869-77.

26. Katagiri R, Asakura K, Kobayashi S, et al. Low Intake of Vegetables, High Intake of Confectionary, and Unhealthy Eating Habits are Associated with Poor Sleep Quality among Middle-aged Female Japanese Workers. *Journal of Occupational Health*, 2014, **56**(5), pp.359-368.

27. Grandner MA, Jackson N, Gerstner JR, et al. Dietary nutrients associated with short and long sleep duration. Data from a nationally representative sample. *Appetite*, 2013, **64**, pp.71-80.

28. Patterson F, Malone SK, Lozano A, et al. Smoking, Screen-Based Sedentary Behavior, and Diet Associated with Habitual Sleep Duration and Chronotype: Data from the UK Biobank. *Annals of Behavioral Medicine*, 2016, **50**(5), pp.715-726.

29. Paine SJ and Gander PH. Differences in circadian phase and weekday/weekend sleep patterns in a sample of middle-aged morning types and evening types. *Chronobiology International*, 2016, **33**(8), pp.1009-1017.

30. Lauderdale DS. Survey Questions About Sleep Duration: Does Asking Separately About Weekdays and Weekends Matter? *Behavioral Sleep Medicine*, 2014, **12**(2), pp.158-168.

31. Day NE, Mckeown N, Wong MY, et al. Epidemiological assessment of diet: a comparison of a 7-day diary with a food frequency questionnaire using urinary markers of nitrogen, potassium and sodium. *International Journal of Epidemiology*, 2001, **30**(2), pp.309-317.

32. Tasali E, Chapotot F, Wroblewski K, et al. The effects of extended bedtimes on sleep duration and food desire in overweight young adults: a home-based intervention. *Appetite*, 2014, **80**, pp.220-4.

33. Duke CH, Williamson JA, Snook KR, et al. Association Between Fruit and Vegetable Consumption and Sleep Quantity in Pregnant Women. *Maternal and Child Health Journal*, 2017, **21**(5), pp.966-973.

34. Lundahl A and Nelson TD. Sleep and food intake: A multisystem review of mechanisms in children and adults. *Journal of Health Psychology*, 2015, **20**(6), pp.794-805.

35. Chaput JP. Sleep patterns, diet quality and energy balance. *Physiology and Behavior*, 2014, **134**, pp.86-91.

36. Peuhkuri K, Sihvola N and Korpela R. Diet promotes sleep duration and quality. *Nutrition Research*, 2012, **32**(5), pp.309-19.

37. Al Khatib HK, Hall WL, Creedon A, et al. Sleep extension is a feasible lifestyle intervention in free-living adults who are habitually short sleepers: a potential strategy for decreasing intake of free sugars? A randomized controlled pilot study. *American Journal of Clinical Nutrition*, 2018, **107**(1), pp.43-53.

38. Lauderdale DS, Knutson KL, Yan LL, et al. Self-reported and measured sleep duration: how similar are they? *Epidemiology*, 2008, **19**(6), pp.838-45.

39. Golley R, Maher C, Matricciani L, et al. Sleep duration or bedtime? Exploring the association between sleep timing behaviour, diet and BMI in children and adolescents. *International Journal of Obesity (2005)*, 2013, **37**(4), pp.546-551.

40. Decastro JM. Social Facilitation of the Spontaneous Meal Size of Humans Occurs on Both Weekdays and Weekends. *Physiology and Behavior*, 1991, **49**(6), pp.1289-1291.

41. The Sleep Council. *The Great British bedtime report* [online]. 2013. [Accessed 18 June 2016]. Available from: https://www.sleepcouncil.org.uk/wp-content/uploads/2013/02/The-Great-British-Bedtime-Report.pdf.

42. Frank S, Gonzalez K, Lee-Ang L, et al. Diet and Sleep Physiology: Public Health and Clinical Implications. *Frontiers in Neurology*, 2017, **8**, p.393.

Chapter 5: Recommended sleep duration is associated with higher consumption of fruits and vegetables; cross-sectional and prospective analyses from the UK Women's Cohort Study

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5.1 Abstract

Background: High intakes of FV has been shown to protect against diseases and all-cause mortality however, the associations between sleep and FV consumption are not well characterized. This study aims to explore both cross-sectional and prospective associations between sleep duration and FV intakes in UK women. This is the first study to demonstrate the prospective association between sleep duration and FV consumption.

Methods: Cross–sectional and prospective data were obtained from the UK Women's Cohort Study. Sleep duration was assessed by self-report of average hours slept on weekdays and weekends and diet was assessed by a 4-day food diary at baseline and follow-up (~4 years later). Sleep duration was categorized as short (≤6 h/d), recommended (7-9 h/d) and long (≥9 h/d). Regression analyses adjusting for age, socio-economic status, smoking, ethnicity and total energy intake were used and restricted cubic spline models were developed to explore potential non-linear associations between sleep duration and FV intakes.

Results: In adjusted cross-sectional analyses, short sleepers had on average 17 g/d (95% CI -30 to-4, $p = 0.01$) and long sleepers had 25 g/d (95% CI -39 to − 12, $p < 0.001$) less total FV compared to recommended sleepers. In adjusted prospective analyses, short sleepers had on average 85 g/d (95% CI -144 to − 26, $p = 0.005$) less total FV in comparison to recommended sleepers. Restricted cubic spline models showed that the cross-sectional ($p < 0.001$) and prospective ($p = 0.001$) associations between sleep duration and FV intakes were non-linear with women sleeping 7-9 h/d having the highest intakes.

Conclusions: FV consumption differed between sleep duration categories with UK women sleeping the recommended 7-9 h/day having the highest intake of FV in cross-sectional and prospective analyses. These findings suggest that sleeping the recommended duration is associated with higher consumption of FV. Sleep is an overlooked lifestyle factor in relation to FV consumption and more notice is vital. Further studies are required to clarify the underlying mechanisms for these associations.

Keywords: Sleep, Fruits and vegetables, Nutritional epidemiology

5.2 Background

Increased consumption of FV protect against diabetes (1), coronary heart disease (2), stroke (3-5) and some cancers (6). The WHO recommends consuming 400 g or more of FV per day to improve overall health and reduce the risk of chronic diseases (7). Recent evidence from a dose-response meta-analysis of prospective studies suggest that the consumption of 800 g per day (10 portions per day) of FV are associated with lower risks of cardiovascular disease, cancer and all-cause mortality (8). Despite these studies, FV consumption remain below the recommended levels (5 portions per day) in the UK (9, 10) and a substantial burden of disease globally is attributable to low consumption (8). Consequently, identifying lifestyle factors, which may influence FV intakes, is a public health priority.

Epidemiological studies have shown that short sleep duration is associated with hypertension (11), type 2 diabetes (12), cardiovascular disease (13) all-cause mortality (14,15) and a 45% increased risk of obesity compared to normal sleep duration (16). These associations may be mediated through changes in dietary intake including FV (17). Several studies have explored the relationship between sleep duration and/or quality and dietary intake in children (18-20) and adolescents (21-24). Shorter sleep duration was associated with higher consumption of energy-rich foods than nutrient dense foods which were FV measured by a FFQ in 10-11 years old children (18). Similarly, longer sleep duration was positively associated with dietary patterns that included FV in Portuguese children aged 5–10 years old (19). In European adolescents, short sleepers (< 8 h/d) consumed less FV compared to those who slept ≥8 h/d (21). Using cross-sectional data from the National Longitudinal Study of Adolescent Health (n = 13,284), short sleep duration (< 7 h/night) was associated with reduced odds of FV consumption compared with the recommended sleep duration (> 8 h/night) (OR 0.66, P < 0.001) (24).

However, this relationship is different in adults due to dissimilar sleep requirements (25). Few studies explored the relationship between sleep measures and FV intakes in adults (26-28) and no prospective study has been done to assess this association. In a retrospective study design, it has been reported that increased hours of sleep in American college students was a significant predictor for higher intakes of FV (26). In a study involving 2000 Japanese workers, short sleepers (< 6 h) consumed fewer vegetables than those sleeping 6-9 h assessed by a dietary habit questionnaire (27). Similar associations were identified in Chinese women from the Shanghai Women's

Health Study (28) that assessed diet using a FFQ; in young female adults from Iran measured diet quality indices (29); and in US adults that assessed FV consumption by average daily servings over the past month (30). The previous studies have shown that sleep duration is associated with dietary intakes and may play an important role in the mediation of association between sleep and health among adults (31). Therefore, there is a need for more studies to assess the longitudinal associations between sleep duration and FV intakes using detailed dietary data (17, 32).

The associations between sleep and dietary intake may be due to multifactorial mechanisms (33-36). These mechanisms include changes in appetite-related hormones ghrelin and leptin (36) due to lack/disrupted sleep that may increase the preference for energy-dense foods (35) leading to potentially lower intakes of FV. Experimental studies suggest that sleep restriction enhances hedonic stimulus processing in the brain and alters brain connectivity leading to food reward, food craving and affecting food decisions (37). The enhanced reward mechanism may mediate energy-dense food consumption leading to lower intakes of FV. These mechanisms have long-term effects on dietary intake (32) which contribute to weight-related outcomes, obesity (16) and other risk factors for the development of chronic diseases such as type 2 diabetes (12) and cardiovascular disease (13). Thus, exploring the prospective associations between sleep measures and FV intakes is essential.

Therefore, this study aims to explore both cross-sectional and prospective associations between sleep duration and FV intakes in women from the UKWCS. To our knowledge, we are the first to report on prospective associations between sleep duration and FV intakes in UK women. This study may clarify whether sleep duration is an attributable factor to low consumptions of fruits and vegetables. We hypothesized that short and long sleep would be associated with lower intakes of FV compared to recommended sleep duration (38).

Methods

5.2.1 Study population

The UKWCS was established to explore links between diet and chronic diseases. Participants were taken from responders to the World Cancer Research Fund's direct mail survey including those living in England, Wales, Scotland and Northern Ireland. Ethical approval was granted at its initiation in 1993 (Research Ethics Committee reference number is 15/YH/0027). The National Research Ethics Committee for

Yorkshire and the Humber, Leeds East has now taken on responsibility for the ongoing cohort. The cohort had two main contact phases; baseline (Phase 1) and follow-up (Phase 2) (Figure 5.1.). Baseline data was not used in this study since sleep duration was only measured in Phase 2. Phase 2 data (1999 to 2002) was obtained by re-contacting the whole cohort and 14,172 (40% of baseline) women aged 33-73 years completed a follow-up health and lifestyle questionnaire which included questions on sleep. A total of 12,453 women (88% of Phase 2 responders) also completed a 4-day food diary and a 1-day activity diary.

Cross-sectional analyses used Phase 2 data for the association between sleep duration and FV intakes. FV biomarker data (vitamin C, α and β carotene and lycopene) also representing cross-sectional information, were used from the non-starch polysaccharide (NSP) intake and serum micronutrient concentrations sub-study conducted during the same period of Phase 2 data collection. The NSP sub-study investigated the associations between NSP intakes and plasma micronutrients in 283 women. NSP fibre and micronutrient intakes were assessed by 4-day food diaries and blood samples were taken and analysed for plasma micronutrient concentrations including carotenoids, vitamin A, vitamin E, thiamine, riboflavin, vitamin B6, vitamin B12, folic acid, and vitamin C and trace metals. The study is described in detail elsewhere (39, 40).

Prospective data were provided from a follow up sub-study (Snacking Study) (39). After ~4 years of Phase 2 (2006), the Snacking sub-study contacted 3596 women from Phase 2 respondents for whom we had not received a notification of death, who had completed a food diary and for whom we had previously captured total eating frequency. A total of 2253 women responded and completed a questionnaire to explore snacking habits with a further 4-day food diary. Sleep duration data from Phase 2 was used as an exposure and FV intake data from the Snacking sub-study was used as an outcome in this prospective analyses.

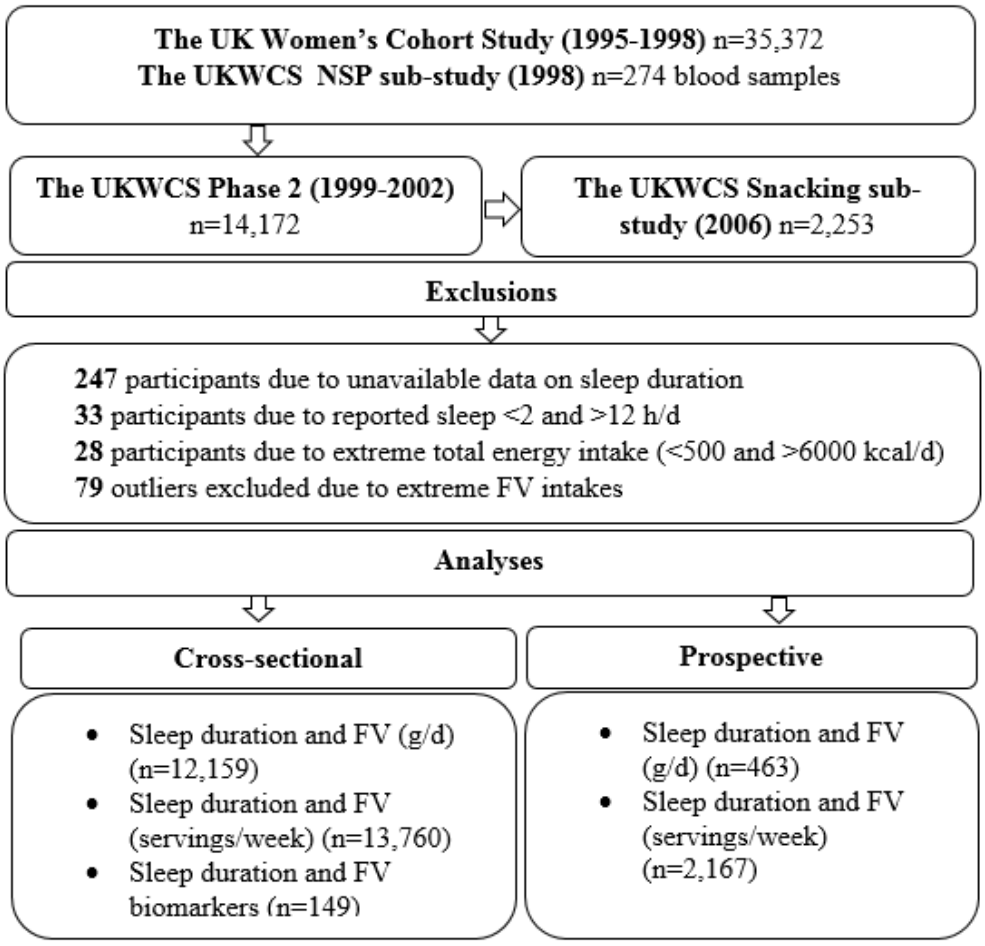


Figure 5.1. Participants flow chart.

Legend: d (day), FV (fruits and vegetables), g (grams), h (hours), n (number), NSP (non-starch polysaccharide), UKWCS (The UK Women's Cohort Study).

5.2.2 Sleep duration

Participants were asked about sleep duration in two separate questions in the following form;

"On an average weekday how is your day spent?"

"On an average weekend how is your day spent?"

Participants were asked to record number of hours and/or minutes that were spent sleeping in an average weekday and weekend (Appendix C (C.2.)). Two separate variables were generated for sleep duration based on weekdays and weekends for all women. Average sleep duration for weekdays and weekends was calculated using the following equation ((minutes slept during the week* 5) + (minutes slept during weekends *2))/7 (41). Sleep duration was categorized to Short Sleepers (SS) (≤6 h/day (≤360 min)),

Recommended Sleepers (7-h/day (> 360min and < 540 min) and Long Sleepers (LS) (≥9 h/day (≥540min)). Sleep duration was used as the exposure variable in both cross-sectional and prospective analyses.

5.2.3 Dietary records

Participants from both the Phase 2 follow up and the Snacking sub-study listed all drinks and foods consumed over 4 days. They were asked to start on a particular day (Friday, Saturday or Sunday) to obtain a range of days of the week. Participants recorded homemade recipes, foods consumed away from home or takeaways and supplement intake. Food records were coded using the Diet and Nutrition Tool for Evaluation (DANTE) (42) that contained standard nutrient intakes from *McCance & Widdowson's The Composition of Foods* (5th Edition) (43) supplementary information from food manufacturers, food labels and homemade recipes. DANTE also contained typical portion sizes for each food derived from *Food Portion Sizes* (44). Total grams of FV per day were obtained from the 4-day food diaries in Phase 2 which was used in the cross-sectional analyses. For prospective analyses, total grams/day of FV intakes were obtained from the 4-day food diaries from the follow-up Snacking sub-study.

Participants were asked in the health and lifestyle questionnaire in Phase 2 and the Snacking sub-study "How many servings of FV or dishes containing FV do you usually eat in an average week?" which were used to obtain servings/week of FV. Total servings/week of FV were the sum of FV. Non-response to FV intakes in the 4-day food diaries and the question in the health and lifestyle questionnaire were taken as missing data.

5.2.4 Biomarkers

Carotenoids and vitamin C levels were measured in the NSP intake and serum micronutrient concentrations sub-study (40). We have chosen these biomarkers based on previous studies that detected their strong correlation with FV consumption (45, 46). Blood was collected at home after an overnight fast. Samples were collected into lithium heparin (8 ml) for carotenoids (α and β-carotene and lycopene) and total vitamin C analysis. Samples were kept cool, separated and prepared for storage at − 70 °C within 2 h of collection. All blood analyses were undertaken in the Division of Pathological Sciences, Department of Clinical Medicine, at the University of Leeds. Antioxidant vitamins were analysed by HPLC as previously described (47).

5.2.5 Phase 2 characteristics

Age, height, weight, medical history, illness history, smoking habits, alcohol consumption frequency and number of children were self-reported. Supplement usage was identified by asking whether participants took any vitamins, minerals, fish oils, fibre or other food supplements. Participants also self-reported their status regarding vegetarian and vegan diets. Physical activity levels were self-reported by asking which activity class best describes their weekly activity (no weekly physical activity, light/moderate physical activity in most weeks, vigorous activity for at least 20 min once or twice a week and vigorous activity at least 20 min three or more times per week). Classification of SES was undertaken based on occupation, according to the NS-SEC, where women are divided into the following categories (never had a paid job, managers and administrators, professional, technical and associate professional, clerical and secretarial, craft and skilled, personal and protective, sales, plant and machine operatives and other) (48). Socio-demographic information such as marital status was determined by self-report questions asking for marital status (married or living as married, divorced, single, widowed, separated).

5.2.6 Statistical analyses

Descriptive statistics such as means and proportions described women from the UKWCS according to sleep duration categories. P values of < 0.05 represent statistical significance. Multiple linear regression analysis was used to assess the relationship between categorical sleep duration and FV intakes in both cross-sectional (data are from Phase 2 and biomarker data are from the NSP sub-study) and prospective analyses (sleep duration data from Phase 2 and FV intake data from the Snacking sub-study). Model 1 included adjustment for age only whereas model 2 was adjusted for potential confounders, identified using a directed acyclic graph. These variables were age, SES (49), smoking (50-53) (yes, no), ethnicity (54, 55) (white, non-white) and total energy intake. We did not feel that there was sufficient experimental evidence that alcohol intake independently influences FV consumption to include alcohol intake as an adjustment. For the same reason we did not adjust for physical activity as there is not sufficient evidence that it independently influences sleep duration and FV consumption.

We used restricted cubic splines to model potential cross-sectional and prospective non-linear relationships between sleep duration as a continuous exposure (h/day) and total FV intakes as the outcomes (g/ d). Cross-sectional, prospective and biomarker splines comprised of 2 polynomial segments separated by 3 knots (at the following percentiles

of sleep duration 10, 50 and 90 as recommended by Harrell (56) with linear regions before the first knot and after the last). P values > 0.05 indicate linearity and < 0.05 indicate non-linearity.

Sensitivity analyses were conducted in the cross-sectional analyses only, due to the smaller number of participants in the prospective analyses. Sensitivity analyses included considering weekdays and weekends separately. Further sensitivity analyses were conducted separately after 1) excluding participants who consumed vitamins, minerals or/and food supplements over the last year, 2) those who self-reported currently having a longstanding illness 3) those taking prescribed medicines; 4) excluding women who self-reported being vegan or vegetarian; 5) BMI was adjusted for in addition to the potential confounders in model 2 as a further sensitivity analysis. Statistical analyses were conducted using IC Stata 14.2 statistical software (57).

5.3 Results

Cohort participants who did not provide information on sleep duration (n = 247) were excluded (Figure 5.1.). Participants who reported sleep duration < 2 or > 12 h/ day (n = 33) were outliers given that adults normally sleep 6-9 h/day and sleeping < 2 or > 12 h/day could indicate illness or an irregular schedule therefore, they were excluded. Participants with extreme total energy intakes (< 500 and > 6000 kcal/day) were excluded from the analyses to minimize errors from under- and over-estimation of intakes (n = 28). Outliers were excluded by removing those who had extreme FV intakes (> 1600 g/d) (n = 20) from the 4-day food diaries, (> 50 servings/week) from the health and lifestyle questionnaire (n = 48) in Phase 2 and the Snacking sub-study (n = 11). The total number of participants in cross-sectional and prospective analyses are shown in Figure 5.1. A total of 12,159 participants in the cross-sectional analyses between sleep duration and FV intakes (grams/day) and 13,760 for FV intakes (servings/week) were included in the analyses. For prospective analyses, 2167 participants were included for FV intakes (servings/week) and 463 participants for FV intakes (grams/day).

5.3.1 Cohort characteristics

The general characteristics of women included from Phase 2 from the UKWCS according to sleep duration category are shown in Table 5.1. (n = 13,925) with a mean age of 52 years (95% CI 52 to 53) and a mean BMI of 24.1(95% CI 24.1 to 24.2). Ten percent of the women (n = 1403) were SS, 81% (n = 11,292) of the women slept the recommended 7-9 hours/day and 9% (n = 1230) of the women were LS. In total, 99% of the women were white (95% CI 98 to 99), 76% (95% CI 75 to 77) of them were married, 8% (95%

CI 7 to 8) of the women reported that they smoke and 32% (95% CI 31 to 33) self-reported being vegetarian or vegan. Recommended sleepers had the highest intakes of FV (g/day) compared to SS and LS. Recommended sleepers had a mean intake of 451 g/d (95% CI 447 to 455) compared to SS who had a mean intake of 430 g/d (95% CI 417 to 442) and LS had a mean intake of 421 g/d (95% CI 409 to 433).

Table 5.1. Participant characteristics, stratified by sleep duration.

Characteristics	Sleep Categories ≤6 hours/day (SS)	7-9hours/day (recommended sleepers)	≥ 9 hours/day (LS)	Total
Observations (n)	1,403	11,292	1,230	13,925
	Mean (95% CI)	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**
Age (years)	55 (54,55)	51 (51,52)	54 (53,54)	52 (52,53)
BMI (kg/m^2)	24.7 (24.5,24.9)	24.0 (23.9,24.1)	24.8 (24.6,25.1)	24.1 (24.1,24.2)
Fruit (g/d)	229 (220,238)	235 (232, 238)	217 (208,226)	232 (229,234)
Vegetables (g/d)	209 (202,215)	222 (219,224)	208 (202, 215)	218 (216,220)
Total fruits and vegetables (g/d)	430 (417,442)	451 (447,455)	421(409,433)	445 (441,448)
Total energy intake (kcal/d)	2329 (2289,2368)	2371(2359,2384)	2331(2293,2368)	2362(2351,2374)
	% (95%CI)	**% (95%CI)**	**% (95%CI)**	**% (95%CI)**
Alcohol consumption frequency (once a week or more)	39 (37,42)	47 (46,48)	37 (34,40)	46 (45, 46)
Has longstanding illness (yes)	33 (31,36)	25 (24,25)	29 (27,32)	26 (25,27)
Taking prescribed medicine (yes)	40 (37,42)	29 (28, 30)	40 (37,43)	31 (30, 32)
Smoking (yes)	10 (9,12)	8 (7,8)	8 (6, 9)	8 (7, 8)
Vitamins, minerals, food supplements (yes)	63 (61,66)	59 (58, 60)	57 (54,60)	60 (59, 61)
Vegetarian or vegan(yes)	33 (30,36)	32 (31, 33)	28 (25,31)	32 (31, 33)
Ethnicity (white)	98 (97, 98)	98 (98, 99)	99 (98,99)	99 (98, 99)
Employer (employed)	47 (45,50)	62 (61,63)	45 (43,48)	59 (58,60)
Socio-economic status (professional)	21 (19,23)	28 (27,29)	26 (24,29)	28 (27,28)
Physical activity (light/moderate)	49 (46,52)	49 (48,50)	56 (53,59)	50 (48,50)
Marital status (married or living as married)	68 (65,70)	77 (76, 78)	77 (75,80)	76 (75,77)
Number of children (2 children)	48 (45, 51)	51 (50,52)	50 (47,53)	50 (49, 51)

Legend: BMI (body mass index), d (day), g (gram), kg (kilogram), LS (long sleepers), m (metre), n (number), SS (short sleepers).

The differences in characteristics between Phase 2 women and Snacking sub-study women are shown in (Appendix E (E.1.)). Women from Phase 2 had a mean age of 52 years whereas women from the Snacking sub-study had a mean age of 51 years (p <0.001). In addition, Phase 2 women had a higher BMI (24.2 kg/m2) than women from the Snacking sub-study (23.6 kg/m2) (p < 0.001). Phase 2 women consumed less grams/day of fruit (225 g/day) compared with Snacking sub-study women who consumed (265 g/day) (p < 0.001) and less grams/day of vegetables (215 g/day) compared with women from the Snacking sub-study who consumed (234 g/day) (p < 0.001). Phase 2 women consumed less grams/day of total FV (435 g/day) compared with Snacking sub-study women who consumed (492 g/day) (p < 0.001). This may be due to the self-report of 29% (n = 3498) of women in Phase 2 being vegetarian or vegan compared with 47% (n = 1043) of women in the Snacking sub-study (p < 0.001). Other characteristics that were significantly different between Phase 2 women and Snacking sub-study women included long-term illness, smoking, supplement intake, employment and physical activity that are shown in (Appendix E (E.1.)).

5.3.2 Cross-sectional analyses between sleep duration and FV intakes

In cross-sectional analyses (model 1) (Table 5.2.), SS had on average 8 g/d (95% CI -18 to 0.8, p = 0.07) less fruit, 10 g/d (95% CI -17 to − 3, p = 0.003) less vegetables and 23 g/d less of total FV (95% CI -36 to − 10, p < 0.001) compared with recommended sleepers. LS had on average 18 g/d less of fruits (95% CI -28 to − 8, p<0.001), 12 g/d less of vegetables (95% CI -19 to − 4, p = 0.001) and 30 g/d (95% CI -43 to − 17, p < 0.001) less of total FV reported in the food diaries compared to recommended sleepers. The questionnaire data showed that SS had on average 0.7 serving/ week less (95% CI -1 to − 0.3, p = 0.001) of fruit, 0.4 serving/ week less of vegetables (95% CI -0.8 to-0.01, p = 0.04) and 1 serving/week less (95% CI -1 to − 0.5, p = 0.001) of total FV compared with recommended sleepers. LS had on average 1 serving/week less (95% CI -1 to − 0.6, p < 0.001) of fruit, 0.04 serving/week less of vegetables (95% CI-0.8,-0.01p = 0.05) and 1 serving/week less (95% CI -2 to − 0.9, p < 0.001) of total FV.

In the fully adjusted cross-sectional analyses (model 2) (Table 5.2.), the food diaries data showed SS had on average 5 g/d (95% CI -15 to 4, p=0.2) less of fruits, 8 g/d (95% CI -15 to − 1, p =0.01) less of vegetables and 17 g/d (95% CI -30 to − 4, p = 0.01) less of total FV compared to recommended sleepers. LS had on average 15 g/d less of fruit (95% CI -25 to − 5, p = 0.003), 11 g/d (95% CI -18 to − 3, p = 0.003) less vegetables and 25 g/d less of total FV (95% CI -39 to − 12, p < 0.001) compared to recommended

sleepers. The questionnaire data showed SS had 0.4 serving/week less (95% CI -0.8 to − 0.02, p = 0.04) of fruits and 0.07 serving/week less (95% CI -1 to − 0.08, p = 0.02) of total FV compared with recommended sleepers. LS had on average 1 serving/ week less (95% CI -1 to − 0.5, p < 0.001) of fruit and 1 serving/week less (95% CI-2 to − 0.6, p < 0.001) of total FV compared with recommended sleepers.

There was no evidence of association between sleep duration and FV biomarker concentrations except for plasma vitamin C that was 4 μg/ml (95% CI -6 to − 1, p = 0.003) lower in short sleepers compared with RS. However, there was a non-linear relationship between sleep duration and plasma vitamin C (p = 0.02) with women sleeping 7-9 h/d having the highest levels compared to SS and LS (Appendix E (E.2.1)). Borderline linearity (p = 0.05) was shown between sleep duration and plasma α-carotene (Appendix E (E.2.2)) and linear associations with plasma β-carotene (Appendix E (E.2.3)) (p = 0.2) and lycopene (Appendix E (E.2.4)) (p = 0.8). Fruit (g/d and servings/week) intakes, vegetable intakes (g/d) and total FV intakes (g/d and servings/week) differed by sleep duration categories.

Table 5.2. Cross-sectional associations between sleep duration categories and FV consumption.

Short sleepers (≤6 h/d) and Long sleepers (≥9 h/d) compared to the recommended group (7-9 h/d)												
Models	**Model 1**						**Model 2**					
Sleep categories	**≤ 6 h/d sleep Mean difference (95% CI)**	**P value**	**≥9 h/d sleep Mean difference (95% CI)**	**P value**	**n**	**Overall P value***	**≤6 h/d sleep Mean difference (95% CI)**	**P value**	**≥9 h/d sleep Mean difference (95% CI)**	**P value**	**n**	**Overall P value***
FV (grams/day)**												
Fruits	-8 (-18,0.8)	0.07	-18 (-28, -8)	<0.001	11,972	<0.001	-5 (-15, 4)	0.2	-15 (-25, -5)	0.003	11,571	0.009
Vegetables	-10 (-17,-3)	0.003	-12 (-19,-4)	0.001	12,148	<0.001	-8 (-15,-1)	0.01	-11 (-18, -3)	0.003	11,738	0.001
Total FV	-23 (-36,-10)	<0.001	-30 (-43, -17)	<0.001	12,159	<0.001	-17 (-30,-4)	0.01	-25 (-39, -12)	<0.001	11,749	<0.001
FV (servings/week)***												
Fruits	-0.7 (-1,-0.3)	0.001	-1 (-1, -0.6)	<0.001	13,623	<0.001	-0.4 (-0.8,-0.02)	0.04	-1 (-1, -0.5)	<0.001	13,127	<0.001
Vegetables	-0.4 (-0.8, -0.01)	0.04	-0.4 (-0.8, -0.01)	0.05	13,660	0.03	-0.3 (-0.7, 0.1)	0.1	-0.3 (-0.8, 0.07)	0.1	13,164	0.1
Total FV	-1 (-1, -0.5)	0.001	-1 (-2, -0.9)	<0.001	13,760	<0.001	-0.7 (-1,-0.08)	0.02	-1 (-2, -0.6)	<0.001	13,260	<0.001
FV biomarkers												
Vitamin C (µg/ml)	-3 (-6,-1)	0.003	2 (-0.03 ,4)	0.05	149	0.001	-4 (-6,-1)	0.003	1 (-0.4,4)	0.1	145	0.001
α-carotene (nmol/l)	-86 (-191,19)	0.1	-54 (-144,36)	0.2	149	0.1	-104 (-219, 9)	0.07	-51 (-150,47)	0.3	145	0.1
β-carotene (nmol/l)	-120 (-542, 302)	0.5	177 (-181,536)	0.3	149	0.5	-120 (-580,340)	0.6	118 (-278, 515)	0.5	145	0.7
Lycopene (nmol/l)	-56 (-223,111)	0.5	113(-29,255)	0.1	148	0.2	-83 (-254, 86)	0.3	107 (-39,254)	0.1	144	0.1

Legend: d (day), FV (fruits and vegetables), h (hour), n (number).
Model 1 adjusted for age
Model 2 adjusted for age, socio-economic status, smoking, ethnicity and total energy intake
* P value for differences between sleep duration categories
** obtained from 4-day food diary
*** obtained from health and lifestyle questionnaire

5.3.3 Prospective analyses between sleep duration and FV intakes

In prospective analyses (model 1) (Table 5.3.), SS had on average 47 g/d less of fruit (95% CI -88 to − 5, p = 0.02), 44 g/d less of vegetables (95% CI -76 to − 12, p = 0.006) and 98 g/d less of total FV (95% CI -155 to − 41, p = 0.001) reported in the food diaries compared with recommended sleepers. LS had on average 8 g/d less of fruit (95% CI -56 to 38, p = 0.7), 9 g/d less of vegetables (95% CI -46 to 26, p= 0.5) and 21 g/d less of total FV (95% CI -87 to 44, p = 0.5). The questionnaire data showed that LS had on average 1 serving/week less of fruit (95% CI -3 to − 0.2, p = 0.02), 0.6 serving/week less of vegetables (95% CI -2 to 0.8, p = 0.4) and 1 serving/week less of total FV (95% CI-3 to − 0.7, p = 0.06) compared with recommended sleepers.

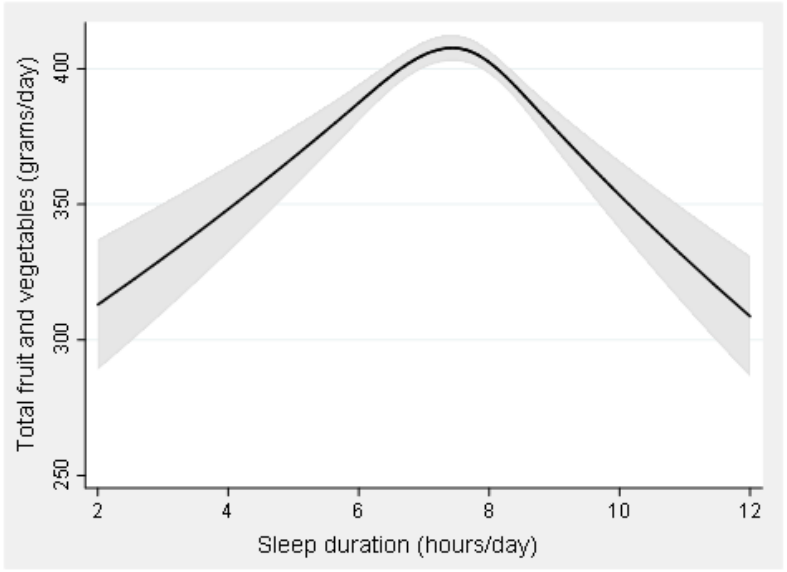
In fully adjusted prospective analyses (model 2) (Table 5.3.), SS had on average 33 g/d less of fruits (95% CI -76 to 9, p=0.1), 44 g/d less of vegetables (95% CI -77 to -11, p=0.008) and 85 g/d less of total FV (95% CI -144 to -26, p=0.005) compared with recommended sleepers from the food diaries. LS had on average 5 g/d less of fruit (95% CI -55 to 44, p=0.8), 22 g/d less of vegetables (95% CI -60 to 15, p=0.2) and 30 g/d less of total FV (95% CI -98 to 38, p=0.3). The questionnaire data showed that LS had on average 1 serving/week less of fruits (95% CI -2 to -0.02, p=0.05), 0.7 serving/week less of vegetables (95% CI -2 to 0.8, p=0.3) and 2 servings/week less of total FV (95% CI -4 to -0.2, p=0.07) compared with recommended sleepers. Total FV intakes (g/d) differed by sleep duration categories.

Table 5.3. Prospective associations between sleep duration categories and FV consumption.

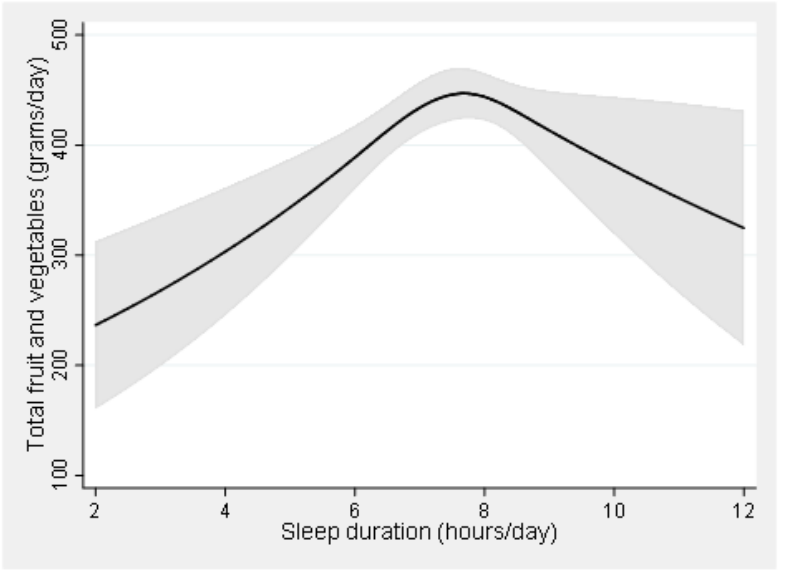
Short sleepers (≤6h/d) and long sleepers (≥9h/d) compared to the recommended group (7-9 h/d)												
Models	**Model 1**						**Model 2**					
	≤6 h/d sleep Mean difference (95% CI)	**P value**	**≥9 h/d sleep Mean difference (95% CI)**	**P value**	**N**	**Overall P value***	**≤6 h/d sleep Mean difference (95% CI)**	**P value**	**≥9 h/d sleep Mean difference (95% CI)**	**P value**	**n**	**Overall P value***
FV(grams/day)**												
Fruits	-47 (-88,-5)	0.02	-8 (-56, 38)	0.7	454	0.08	-33 (-76,9)	0.1	-5 (-55, 44)	0.8	440	0.3
Vegetables	-44 (-76,-12)	0.006	-9 (-46,26)	0.5	462	0.02	-44 (-77,-11)	0.008	-22 (-60,15)	0.2	448	0.01
Total FV	-98 (-155,-41)	0.001	-21 (-87,44)	0.5	463	0.003	-85(-144,-26)	0.005	-30 (-98,38)	0.3	449	0.01
FV (servings/week)***												
Fruits	-0.6 (-2, 0.6)	0.3	-1 (-3,-0.2)	0.02	2,162	0.05	-0.4 (-1, 0.8)	0.5	-1 (-2,0.02)	0.05	2,087	0.1
Vegetables	-0.6 (-1, 0.7)	0.3	-0.6 (-2,0.8)	0.4	2,169	0.5	-0.4 (-1, 0.9)	0.5	-0.7 (-2, 0.8)	0.3	2,094	0.5
Total FV	-1 (-3, 0.7)	0.2	-2 (-4,0.1)	0.06	2,167	0.1	-0.9 (-3, 1)	0.3	-2 (-4, 0.2)	0.07	2,092	0.1

Legend: d (day), FV (fruits and vegetables), h (hour), n (number)
Model 1 adjusted for age
Model 2 adjusted for age, socio-economic status, smoking, ethnicity and total energy intake
* P value for differences between sleep duration categories
** obtained from 4-day food diary
*** obtained from health and lifestyle questionnaire

Restricted cubic spline modelling showed that the cross-sectional (Figure 5.2.A.) ($p < 0.001$) and prospective (Figure 5.2.B) ($p = 0.001$) associations between sleep duration and total FV intakes (g/d) were non-linear with women sleeping 7–9 h/d having the highest intakes of total FV compared to SS and LS.



5.2.A Cross-sectional



5.2.B Prospective

Figure 5.2. Associations between sleep duration and total intakes of FV from the restricted cubic spline modelling.

Legend: Black lines plot the predicted cross-sectional (5.2.A) and prospective (5.2.B) intakes of total FV values with 95% confidence intervals (grey shaded area) for all women from the UKWCS.

5.3.4 Sensitivity analyses

Sensitivity analyses showed broadly similar results (Appendix E (E.3. - E.8.). After excluding supplement users (n = 7776) (Appendix E (E.3.)), LS had 14 g/d less of fruit (95% CI -28 to − 0.5, p= 0.04), 21 g/d less of vegetables (95% CI -31 to − 10, p < 0.001) and 33 g/d less of total FV (95% CI -53 to − 14, p = 0.001) compared with recommended sleepers. In addition, LS had on average 1 serving/week less of fruit (95% CI -1 to − 0.5, p < 0.001), 0.8 serving/week less of vegetables (95% CI -1 to − 0.1, p = 0.01) and 1 serving/week less of total FV (95% CI -3 to − 0.9, p < 0.001) compared with recommended sleepers No significant difference between SS and RS was observed and fruit, vegetable and total FV intakes (g/d and servings/week) differed between sleep duration categories.

After excluding participants who reported being vegan or/and vegetarian (n = 4541) (Appendix E (E.4.)), SS had on average 10 g/ d less of vegetables (95% CI-18 to − 2, p= 0.008) and 17 g/d less of total FV (95% CI -32 to − 2, p = 0.02). LS had on average 12 g/d less of fruit (95% CI -23 to − 1, p = 0.02), 10 g/d less of vegetables (95% CI -18 to − 3, p = 0.007) and 24 g/d less of total FV (95% CI -39 to − 9, p = 0.001) compared with recommended sleepers. Similar results were shown for questionnaire data and total FV intakes (g/d and servings/week) differed between sleep duration categories. Similar results were observed after separately excluding women who reported having a longstanding illness (n = 3753) (Appendix E (E.5.)), those who reported long term treatments for illness (n = 4252) (Appendix E (E.6.)) and after including adjustment for BMI in the fully adjusted model (Appendix E (E.7.)).

After considering sleep duration separately on weekdays and weekends (Appendix E (E.8.), SS had 13 g/d less of total FV on weekdays (95% CI -25 to − 0.9, p = 0.03). LS on weekdays had 18 g/d less of fruit (95% CI -23 to − 8, p < 0.001), 10 g/d less of vegetables (95% CI -18 to − 3, p = 0.003) and 29 g/d less of total FV (95% CI -42 to − 16, p < 0.001). Similar results were shown for the questionnaire data. Weekend sleep duration categories showed that LS had on average 16 g/d less of fruits (95% CI -23 to − 9, p < 0.001), 9 g/d less of vegetables (95% CI -14 to − 4, p < 0.001) and 26 g/d less of total FV (95% CI -36 to − 17, p < 0.001). No difference was observed in FV intakes between SS and RS on weekend days.

5.4 Discussion

This study is the first to report both cross-sectional and prospective associations between sleep duration and FV intakes in middle-aged UK women. The results were consistent in

cross-sectional and prospective associations with SS and LS having fewer grams and servings of FV compared with recommended sleepers. No associations were found between sleep duration and FV biomarkers except for plasma vitamin C that was lower in SS compared with RS (Table 5.2.). FV intakes differed between sleep duration categories indicating that sleep duration may predict FV consumption. Although there is poor agreement between both assessment methods of FV intakes (4-day diaries and questionnaires) (58) and dissimilar characteristics between women from Phase 2 and the Snacking Sub-study (Appendix E (E.1.)), the results remained consistent with SS and LS consuming less FV compared with recommended sleepers providing consistency for the observed associations. The cross-sectional and prospective associations between sleep duration and FV intakes were significantly non-linear with RS having the highest intakes compared to SS and LS as confirmed by the restricted cubic spline modelling. These results were supported with the non-linear association between sleep duration and plasma vitamin C shown in the restricted cubic spline model (Appendix E (E.2.)). Collectively, these findings suggest that among UK women, those sleeping the recommended 7-9 h/d have the highest intakes of FV compared to both SS and LS.

Our findings for UK women are in line with several cross-sectional studies from other countries (59-62). Among American women within 5 years of childbirth, LS (≥ 9 h) had lower quality diet, lower consumption of total fruit and whole fruit compared to adequate sleepers (59). Similarly, a study of 27,983 women from the USA or Puerto Rico showed that women with long sleep durations (≥ 10 h) compared to shorter (< 6 h) were less likely to eat during conventional eating hours and more likely to snack which was related to lower intakes of FV (60). A cross-sectional study conducted with 439,933 adults in the UK Biobank project assessing FV intakes in the previous year by asking how many pieces of fresh fruit participants ate per day and how many heaped table-spoons of vegetables participants ate on average per day (61) whereas, our study assessed FV intakes using the 4-day food diaries. Their results were consistent with some of the findings in this study; longer sleep duration (≥9 h) was negatively associated with daily fruit intake and positively associated with vegetable intake unlike our results that found an inverse u-shaped association in vegetable intake between sleep duration groups.

Although the UKWCS does not represent the UK population, the results were consistent with our recent analyses conducted between sleep duration and FV intakes using the more recent NDNS aiming to be representative of both men and women in the UK population (41). SS and LS had lower intakes of fruit and total FV (grams/day) compared

with the reference group (7-8 h/d). The NDNS results showed SS having lower levels of plasma FV biomarkers compared with RS whereas this study only found lower levels of plasma vitamin C however, biomarker data (n = 145) was low compared to the number of participants with 4 day diaries (n = 12,159) and may be the reason of why no other associations were found between sleep duration and biomarkers. These results were supported by Beydoun et al. among US adults however, sleep measures were the outcomes (63). When SS (5-6 h) were compared to normal sleepers (7-8 h), total carotenoid concentration was linked to increased risk of short sleep.

Several cross-sectional studies reported low consumption of FV in SS only (29, 30, 64, 65) whereas we also found lower FV intakes in LS. This might be explained by differences in methods of dietary assessment between studies such as FFQ (29), brief diet history questionnaire (64) or self-report of FV consumption in the previous month (30, 65). The UKWCS used a four-day food diary which is considered a better estimate of average intakes compared to other dietary assessment methods and was also used in the NDNS (41). Furthermore, different population characteristics such as sex, region (66, 67) and genes (67, 68) need to be considered in comparison to the UKWCS results. Sex differences in sleep are mainly driven by biological factors and hormonal differences (66). This study was conducted in middle-aged women only that may have undergone distinct hormonal and physical changes at specific time points such as puberty (69), pregnancy (70), menopause and menstrual cycle phase (71) that may have impacts on their sleep. However, it is important to note that our sample are more health conscious given the number of vegetarians and the professional SES as shown in the descriptive table (Table 5.1.) compared to the general population. Collectively, these conflicting results may be due to different categorization of sleep duration (17). Therefore, this study used the restricted cubic splines models with sleep duration as a continuous variable.

The prospective non-linear association in this study confirmed the cross-sectional non-linear association in the UKWCS and the NDNS (41) with recommended sleepers having the highest intakes of FV compared with SS and LS. However, it is important to note that the presented study needs further confirmation due to the methodologies used in this study. Sleep duration was based on self-report and the dietary assessment method was not validated and does not represent a typical week. Larger prospective and interventional studies are required to support our results using objective assessment methods of sleep measures and a validated dietary assessment tool that represents a typical week (e.g. 7-day food diary) instead of 4 consequent days that included weekends

which differ in dietary intakes compared to weekdays (72, 73). In addition, further research is essential to understand the mechanisms underlying the association of RS having the highest intakes of FV.

Several mechanisms may underlie the association between SS and LS having low intakes of FV in this study (17, 35, 36, 38), although not measured in this study. These mechanisms include hormonal (such as ghrelin and leptin) (17, 36) and behavioural (35, 36) (preference for energy dense foods) changes that lead to low intakes of FV. Recently, long sleep duration is proposed to impair energy metabolism and increase the risk of obesity and type 2 diabetes through possible mechanisms including poor sleep quality, sedentary lifestyle, unhealthy dietary choices and desynchrony between circadian and behavioural states related to exposure of evening artificial light that may delay circadian phase and sleep onset (38). Similarly, longer sleep durations have been associated with increased mortality and incident of cardiovascular disease in a dose-response meta-analyses (74).

Several experimental sleep restriction studies in healthy adults (75) and at risk of obesity adults (76) reported lower fat and carbohydrate intake when transitioned from sleep restriction to adequate sleep (75) and lower overall appetite and desire for energy-dense food when sleep was extended to 8.5 h for 2 weeks (76). Additionally, a recent randomised controlled pilot study suggested the feasibility of sleep extension intervention in habitually SS free-living adults (77). The results showed decreased intake of free sugars in the intervention group (4 weeks) compared to control which provides insight that sleep extension has an impact on dietary intakes. The previous experimental studies extended sleep duration to the recommended hours however, current evidence suggests that long sleep duration have similar effects on diet as lack of sleep (32, 38) which was observed in the results of this study. It seems a public health message to increase sleep may not have the desired effect if adults sleeping the recommended hours move towards long sleep duration (38). Long-intervention studies comparing SS and LS with RS are required for a deeper understanding of the interactions between sleep and FV intakes. On the other hand, sleep is promoted by foods that have an impact on the availability of tryptophan and the synthesis of serotonin and melatonin (78). Some studies indicated that tart cherries (79) and kiwifruits (80) promote sleep due to their high content of antioxidants and serotonin providing insight to the relationship between sleep and diet being potentially reciprocal (32).

According to The Sleep council, sleep duration have been declining with 70% of UK adults sleeping less than 7 h per night (81) and only 30% of UK adults met the 5-a-day recommendation according to Public Health England (9,10). These trends highlight the importance of translating the scientific evidence focusing on the relationship between sleep and diet into practical messages that can help the public to prevent chronic diseases. More information on the integral relationship between sleep and diet may be included in national dietary guidelines for different populations to enhance healthy lifestyle recommendations. If our results are confirmed by interventional studies, the relationship between sleep and FV consumption can be incorporated in weight-loss programs and those that target improvement in overall health (32).

5.4.1 Strengths and limitations

This study has several limitations that need to be considered when interpreting the results. Diet was assessed using 4-day food diaries starting on a particular day (Friday, Saturday or Sunday) to obtain a range of days of the week however, these days are not representative of a typical week. The self-report of sleep duration was based on memory which could lead to over-reporting (82) and no questions regarding sleep disorders or parameters were included. Further limitations include lack of consideration of other factors of sleep that may have an impact on the relationship between sleep and FV intakes such as sleep quality (83,84) sleep timing (22) and chronotype (55,61). Other factors include daytime and night time light exposure (85), shift work (85), daytime napping was also not considered in this study and seasonal variation (86) that may affect sleep duration. The smaller number of participants in the prospective analyses was a further limitation. On the other hand, our analyses has several strengths. The UKWCS is a large prospective cohort which includes health-conscious women with a wide diversity in dietary intakes and a large number of participants were included in the cross-sectional analyses which facilitates in clarifying the associations between sleep duration and FV intakes. Furthermore, to our knowledge this is the first study that had investigated the prospective associations between sleep duration and FV intakes.

5.5 Conclusion

Evidence from this study suggest that a sub-group of UK women sleeping the recommended 7-9 h/d had the highest intakes of FV compared with SS and LS indicating that sleep duration may predict the intake of FV. Our findings support the accumulating evidence showing an important contribution of sleep duration to dietary intake.

References of Chapter 5

1. Muraki I, Imamura F, Manson JE, et al. Fruit consumption and risk of type 2 diabetes: results from three prospective longitudinal cohort studies. *BMJ*, 2013, **347**, p.f5001.

2. He F, Nowson C, Lucas M, et al. Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies. *Journal of Human Hypertension*, 2007, **21**(9), pp.717-728.

3. Dauchet L, Amouyel P and Dallongeville J. Fruit and vegetable consumption and risk of stroke - A meta-analysis of cohort studies. *Neurology*, 2005, **65**(8), pp.1193-1197.

4. He FJ, Nowson CA and Macgregor GA. Fruit and vegetable consumption and stroke: meta-analysis of cohort studies. *Lancet*, 2006, **367**(9507), pp.320-326.

5. Hu D, Huang J, Wang Y, et al. Fruits and vegetables consumption and risk of stroke: a meta-analysis of prospective cohort studies. *Stroke*, 2014, **45**(6), pp.1613-9.

6. World Cancer Research Fund / American Institute for Cancer Research. *Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective.* [online]. 2007. [Accessed 10 November 2015]. Available from: http://discovery.ucl.ac.uk/4841/1/4841.pdf.

7. WHO. *Diet, nutrition and the prevention of chronic diseases* [online]. 2003. [Accessed 19 May 2017]. Available from: http://apps.who.int/iris/bitstream/handle/10665/42665/WHO_TRS_916.pdf?sequence=1.

8. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies. *International Journal of Epidemiology*, 2017, **46**(3), pp.1029-1056.

9. Bates B, Lennox A, Prentice A, et al. *National Diet and Nutrition Survey Results from years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009-2011/2012).* [online]. 2014. [Accessed 20 June 2017]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/594361/NDNS_Y1_to_4_UK_report_full_text_revised_February_2017.pdf.

10. Roberts C, Steer T, Maplethorpe N, et al. *National Diet and Nutrition Survey Results from years 7 and 8 (combined) of the Rolling Programme (2014/2015 to 2015/2016).* [online]. 2018. [Accessed 17 October 2017]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/699241/NDNS_results_years_7_and_8.pdf.

11. Stranges S, Dorn JM, Cappuccio FP, et al. A population-based study of reduced sleep duration and hypertension: the strongest association may be in premenopausal women. *Journal of Hypertension*, 2010, **28**(5), pp.896-902.

12. Chaput JP, Despres JP, Bouchard C, et al. Association of sleep duration with type 2 diabetes and impaired glucose tolerance. *Diabetologia*, 2007, **50**(11), pp.2298-304.

13. Cappuccio FP, Cooper D, D'elia L, et al. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *European Heart Journal*, 2011, **32**(12), pp.1484-92.

14. Cappuccio FP, D'elia L, Strazzullo P, et al. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. *Sleep*, 2010, **33**(5), pp.585-92.

15. Yin J, Jin X, Shan Z, et al. Relationship of Sleep Duration With All-Cause Mortality and Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies. *Journal of the American Heart Association*, 2017, **6**(9).

16. Wu Y, Zhai L and Zhang D. Sleep duration and obesity among adults: a meta-analysis of prospective studies. *Sleep Medicine*, 2014, **15**(12), pp.1456-62.

17. Dashti HS, Scheer FA, Jacques PF, et al. Short sleep duration and dietary intake: epidemiologic evidence, mechanisms, and health implications. *Advances in Nutrition*, 2015, **6**(6), pp.648-59.

18. Westerlund L, Ray C and Roos E. Associations between sleeping habits and food consumption patterns among 10-11-year-old children in Finland. *British Journal of Nutrition*, 2009, **102**(10), pp.1531-7.

19. Moreira P, Santos S, Padrao P, et al. Food patterns according to sociodemographics, physical activity, sleeping and obesity in Portuguese children. *International Journal of Environmental Research and Public Health*, 2010, **7**(3), pp.1121-38.

20. Shi Z, Taylor AW, Gill TK, et al. Short sleep duration and obesity among Australian children. *BMC Public Health*, 2010, **10**(1).

21. Garaulet M, Ortega FB, Ruiz JR, et al. Short sleep duration is associated with increased obesity markers in European adolescents: effect of physical activity and dietary habits. The HELENA study. *International Journal of Obesity (2005)*, 2011, **35**(10), pp.1308-17.

22. Golley R, Maher C, Matricciani L, et al. Sleep duration or bedtime? Exploring the association between sleep timing behaviour, diet and BMI in children and adolescents. *International Journal of Obesity (2005)*, 2013, **37**(4), pp.546-551.

23. Beebe DW, Simon S, Summer S, et al. Dietary intake following experimentally restricted sleep in adolescents. *Sleep*, 2013, **36**(6), pp.827-34.

24. Kruger AK, Reither EN, Peppard PE, et al. Do sleep-deprived adolescents make less-healthy food choices? *British Journal of Nutrition*, 2014, **111**(10), pp.1898-904.

25. Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*, 2015, **1**(1), pp.40-43.

26. Adams TB and Colner W. The association of multiple risk factors with fruit and vegetable intake among a nationwide sample of college students. *Journal of American College Health*, 2008, **56**(4), pp.455-61.

27. Imaki M, Hatanaka Y, Ogawa Y, et al. An epidemiological study on relationship between the hours of sleep and life style factors in japanese factory workers. *Journal of Physiological Anthropology and Applied Human Science*, 2002, **21**(2), pp.115-120.

28. Tu X, Cai H, Gao YT, et al. Sleep duration and its correlates in middle-aged and elderly Chinese women: the Shanghai Women's Health Study. *Sleep Medicine*, 2012, **13**(9), pp.1138-45.

29. Haghighatdoost F, Karimi G, Esmaillzadeh A, et al. Sleep deprivation is associated with lower diet quality indices and higher rate of general and central obesity among young female students in Iran. *Nutrition*, 2012, **28**(11-12), pp.1146-50.

30. Stamatakis KA and Brownson RC. Sleep duration and obesity-related risk factors in the rural Midwest. *Preventive Medicine*, 2008, **46**(5), pp.439-44.

31. St-Onge M-P, Crawford A and Aggarwal B. Plant-Based Diets: Reducing Cardiovascular Risk by Improving Sleep Quality? *Current Sleep Medicine Reports*, 2018, **4**(1), pp.74-78.

32. Frank S, Gonzalez K, Lee-Ang L, et al. Diet and Sleep Physiology: Public Health and Clinical Implications. *Frontiers in Neurology*, 2017, **8**, p.393.

33. Knutson KL, Spiegel K, Penev P, et al. The metabolic consequences of sleep deprivation. *Sleep Medicine Reviews*, 2007, **11**(3), pp.163-78.

34. Patel SR and Hu FB. Short sleep duration and weight gain: a systematic review. *Obesity (Silver Spring)*, 2008, **16**(3), pp.643-53.

35. Chaput JP. Sleep patterns, diet quality and energy balance. *Physiology and Behavior*, 2014, **134**, pp.86-91.

36. Lundahl A and Nelson TD. Sleep and food intake: A multisystem review of mechanisms in children and adults. *Journal of Health Psychology*, 2015, **20**(6), pp.794-805.

37. St-Onge MP, Wolfe S, Sy M, et al. Sleep restriction increases the neuronal response to unhealthy food in normal-weight individuals. *International Journal of Obesity (2005)*, 2014, **38**(3), pp.411-6.

38. Tan X, Chapman CD, Cedernaes J, et al. Association between long sleep duration and increased risk of obesity and type 2 diabetes: A review of possible mechanisms. *Sleep Medicine Reviews*, 2018, **40**, pp.127-134.

39. Cade JE, Burley VJ, Alwan NA, et al. Cohort Profile: The UK Women's Cohort Study (UKWCS). *International Journal of Epidemiology*, 2017, **46**(2), p.e11.

40. Greenwood DC, Cade JE, White K, et al. The impact of high non-starch polysaccharide intake on serum micronutrient concentrations in a cohort of women. *Public Health Nutrition*, 2004, **7**(4), pp.543-8.

41. Noorwali EA, Cade JE, Burley VJ, et al. The relationship between sleep duration and fruit/vegetable intakes in UK adults: a cross-sectional study from the National Diet and Nutrition Survey. *Bmj Open*, 2018, **8**(4), p.e020810.

42. Dahm CC, Keogh RH, Spencer EA, et al. Dietary Fiber and Colorectal Cancer Risk: A Nested Case-Control Study Using Food Diaries. *Journal of the National Cancer Institute*, 2010, **102**(9), pp.614-626.

43. Holland BEA. *McCance and Widdowson's the Composition of Foods. 6th edition. Cambridge: Royal Society of Chemistry; 2002.* 5th ed. London: Royal Society of Chemistry and Ministry of Agriculture, Fisheries and Food., 1991.

44. Crawley H. *Food Portion Sizes.* 2nd ed. London: HMSO, 1993.

45. Al-Delaimy WK, Slimani N, Ferrari P, et al. Plasma carotenoids as biomarkers of intake of fruits and vegetables: ecological-level correlations in the European Prospective Investigation into Cancer and Nutrition (EPIC). *European Journal of Clinical Nutrition*, 2005, **59**(12), pp.1397-1408.

46. Souverein OW, De Vries JHM, Freese R, et al. Prediction of fruit and vegetable intake from biomarkers using individual participant data of diet-controlled intervention studies. *British Journal of Nutrition*, 2015, **113**(9), pp.1396-1409.

47. Thurnham DI, Smith E and Flora PS. Concurrent Liquid-Chromatographic Assay of Retinol, Alpha-Tocopherol, Beta-Carotene, Alpha-Carotene, Lycopene, and Beta-Cryptoxanthin in Plasma, with Tocopherol Acetate as Internal Standard. *Clinical Chemistry*, 1988, **34**(2), pp.377-381.

48. Office for National Statistics. *The National Statistics Socio-economic classification (NS-SEC)* [online]. [Accessed 28 November 2016]. Available from: https://www.ons.gov.uk/methodology/classificationsandstandards/otherclassifications/thenationalstatisticssocioeconomicclassificationnssecrebasedonsoc2010.

49. Office for National Statistics. *SOC2010 volume 3: the National Statistics Socio-economic classification (NS-SEC rebased on SOC2010)* [online]. [Accessed 20 November 2015]. Available from: https://www.ons.gov.uk/methodology/classificationsandstandards/standardoccupationalclassificationsoc/soc2010/soc2010volume3thenationalstatisticssocioeconomicclassificationnssecrebasedonsoc2010.

50. Zhang L, Samet J, Caffo B, et al. Cigarette smoking and nocturnal sleep architecture. *American Journal of Epidemiology*, 2006, **164**(6), pp.529-37.

51. Jaehne A, Unbehaun T, Feige B, et al. How smoking affects sleep: a polysomnographical analysis. *Sleep Medicine*, 2012, **13**(10), pp.1286-92.

52. Lohse T, Rohrmann S, Bopp M, et al. Heavy Smoking Is More Strongly Associated with General Unhealthy Lifestyle than Obesity and Underweight. *PloS One*, 2016, **11**(2).

53. Palaniappan U, Starkey LJ, O'loughlin J, et al. Fruit and vegetable consumption is lower and saturated fat intake is higher among Canadians reporting smoking. *Journal of Nutrition*, 2001, **131**(7), pp.1952-1958.

54. Grandner MA, Patel NP, Jean-Louis G, et al. Sleep-Related Behaviors and Beliefs Associated With Race/Ethnicity in Women. *Journal of the National Medical Association*, 2013, **105**(1), pp.4-15.

55. Bei B, Wiley JF, Trinder J, et al. Beyond the mean: A systematic review on the correlates of daily intraindividual variability of sleep/wake patterns. *Sleep Medicine Reviews*, 2016, **28**, pp.108-124.

56. Harrell F. *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis.* New York Springer, 2001.

57. Stata Statistical Software: Release 15; StataCorp LLC: College Station, TX, USA, 2017.

58. Day NE, Mckeown N, Wong MY, et al. Epidemiological assessment of diet: a comparison of a 7-day diary with a food frequency questionnaire using urinary markers of nitrogen, potassium and sodium. *International Journal of Epidemiology*, 2001, **30**(2), pp.309-317.

59. Xiao RS, Moore Simas TA, Pagoto SL, et al. Sleep Duration and Diet Quality Among Women Within 5 Years of Childbirth in the United States: A Cross-Sectional Study. *Maternernal and Child Health Journal*, 2016, **20**(9), pp.1869-77.

60. Kim S, Deroo LA and Sandler DP. Eating patterns and nutritional characteristics associated with sleep duration. *Public Health Nutrition*, 2011, **14**(5), pp.889-95.

61. Patterson F, Malone SK, Lozano A, et al. Smoking, Screen-Based Sedentary Behavior, and Diet Associated with Habitual Sleep Duration and Chronotype: Data from the UK Biobank. *Annals of Behavioral Medicine*, 2016, **50**(5), pp.715-726.

62. Mossavar-Rahmani Y, Jung M, Patel SR, et al. Eating behavior by sleep duration in the Hispanic Community Health Study/Study of Latinos. *Appetite*, 2015, **95**, pp.275-84.

63. Beydoun MA, Gamaldo AA, Canas JA, et al. Serum nutritional biomarkers and their associations with sleep among US adults in recent national surveys. *PloS One*, 2014, **9**(8), p.e103490.

64. Komada Y, Narisawa H, Ueda F, et al. Relationship between Self-Reported Dietary Nutrient Intake and Self-Reported Sleep Duration among Japanese Adults. *Nutrients*, 2017, **9**(2).

65. Duke CH, Williamson JA, Snook KR, et al. Association Between Fruit and Vegetable Consumption and Sleep Quantity in Pregnant Women. *Maternal and Child Health Journal*, 2017, **21**(5), pp.966-973.

66. Nowakowski S, Meers J and Heimbach E. Sleep and Women's Health. *Sleep Medicine Research*, 2013, **4**(1), pp.1-22.

67. Tang JS, Liao YH, Kelly BC, et al. Gender and Regional Differences in Sleep Quality and Insomnia: A General Population-based Study in Hunan Province of China. *Scientific Reports*, 2017, **7**, p.43690.

68. Dashti HS, Follis JL, Smith CE, et al. Habitual sleep duration is associated with BMI and macronutrient intake and may be modified by CLOCK genetic variants. *American Journal of Clinical Nutrition*, 2015, **101**(1), pp.135-43.

69. Hagenauer MH, Perryman JI, Lee TM, et al. Adolescent Changes in the Homeostatic and Circadian Regulation of Sleep. *Developmental Neuroscience*, 2009, **31**(4), pp.276-284.

70. Hedman C, Pohjasvaara T, Tolonen U, et al. Effects of pregnancy on mothers' sleep. *Sleep Medicine*, 2002, **3**(1), pp.37-42.

71. Leroux A, Wright L, Perrot T, et al. Impact of menstrual cycle phase on endocrine effects of partial sleep restriction in healthy women. *Psychoneuroendocrinology*, 2014, **49**, pp.34-46.

72. Yang PHW, Black JL, Barr SI, et al. Examining differences in nutrient intake and dietary quality on weekdays versus weekend days in Canada. *Applied Physiology Nutrition and Metabolism*, 2014, **39**(12), pp.1413-1417.

73. An RP. Weekend-weekday differences in diet among US adults, 2003-2012. *Annals of Epidemiology*, 2016, **26**(1), pp.57-65.

74. Jike M, Itani O, Watanabe N, et al. Long sleep duration and health outcomes: A systematic review, meta-analysis and meta-regression. *Sleep Medicine Reviews*, 2018, **39**, pp.25-36.

75. Markwald RR, Melanson EL, Smith MR, et al. Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. *Proceedings of the National Academy of Sciences of the United States of America*, 2013, **110**(14), pp.5695-700.

76. Tasali E, Chapotot F, Wroblewski K, et al. The effects of extended bedtimes on sleep duration and food desire in overweight young adults: a home-based intervention. *Appetite*, 2014, **80**, pp.220-4.

77. Al Khatib HK, Hall WL, Creedon A, et al. Sleep extension is a feasible lifestyle intervention in free-living adults who are habitually short sleepers: a potential strategy for decreasing intake of free sugars? A randomized controlled pilot study. *American Journal of Clinical Nutrition*, 2018, **107**(1), pp.43-53.

78. Peuhkuri K, Sihvola N and Korpela R. Diet promotes sleep duration and quality. *Nutrition Research*, 2012, **32**(5), pp.309-19.

79. Pigeon W, Carr M, Gorman C, et al. Effects of a Tart Cherry Juice Beverage on the Sleep of Older Adults with Insomnia: A Pilot Study. *Journal of Medicinal Food*, 2010, **13**(3), pp.579-583.

80. Lin H, Tsai P, Fang S, et al. Effect of kiwifruit consumption on sleep quality in adults with sleep problems. *Asia Pacific Journal of Clinical Nutrition*, 2011, **20**(2), pp.169-74.

81. The Sleep Council. *The Great British bedtime report* [online]. 2013. [Accessed 7 September 2016]. Available from: https://www.sleepcouncil.org.uk/wp-content/uploads/2013/02/The-Great-British-Bedtime-Report.pdf.

82. Lauderdale DS, Knutson KL, Yan LL, et al. Self-reported and measured sleep duration: how similar are they? *Epidemiology*, 2008, **19**(6), pp.838-45.

83. Katagiri R, Asakura K, Kobayashi S, et al. Low Intake of Vegetables, High Intake of Confectionary, and Unhealthy Eating Habits are Associated with Poor Sleep Quality among Middle-aged Female Japanese Workers. *Journal of Occupational Health*, 2014, **56**(5), pp.359-368.

84. Hoefelmann LP, Lopes Ada S, Silva KS, et al. Lifestyle, self-reported morbidities, and poor sleep quality among Brazilian workers. *Sleep Medicine*, 2012, **13**(9), pp.1198-201.

85. Potter GD, Skene DJ, Arendt J, et al. Circadian Rhythm and Sleep Disruption: Causes, Metabolic Consequences, and Countermeasures. *Endocrine Reviews*, 2016, **37**(6), pp.584-608.

86. Allebrandt KV, Teder-Laving M, Kantermann T, et al. Chronotype and sleep duration: the influence of season of assessment. *Chronobiology International*, 2014, **31**(5), pp.731-40

Chapter 6: Discussion, directions for future work and conclusions

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6.1 Summary of project contributions to existing knowledge

The reciprocal relationship between sleep disruption and diet were evident before this project began. However, the literature review identified novel gaps that are important to address. Several of these gaps were answered in the previous four chapters that are relevant to public health:

- **In Chapter 2**, cross-sectional analyses, we found that every hour later of mid-sleep time (chronotype) was associated with 16% lower intakes of total fruit in UK adults.
- **In Chapter 3,** prospective analyses, we found that FV consumption (exposure) and their polyphenol content were inversely associated with sleep duration in UK women.
- **In Chapter 4,** cross-sectional analyses, sleep duration (exposure) was non-linearly associated with FV consumption from a nationally representative database of UK adults.
- **In Chapter 5,** cross-sectional and prospective analyses, sleep duration (exposure) was non-linearly associated with FV consumption. UK women sleeping the recommended 7-9 hours/day had the highest intakes of FV compared to short and long sleepers.

In this final chapter I will summarise project findings (Figure 6.1) and their implications for public health. I will discuss project strengths and limitations and suggest ideas for future studies to build on this work.

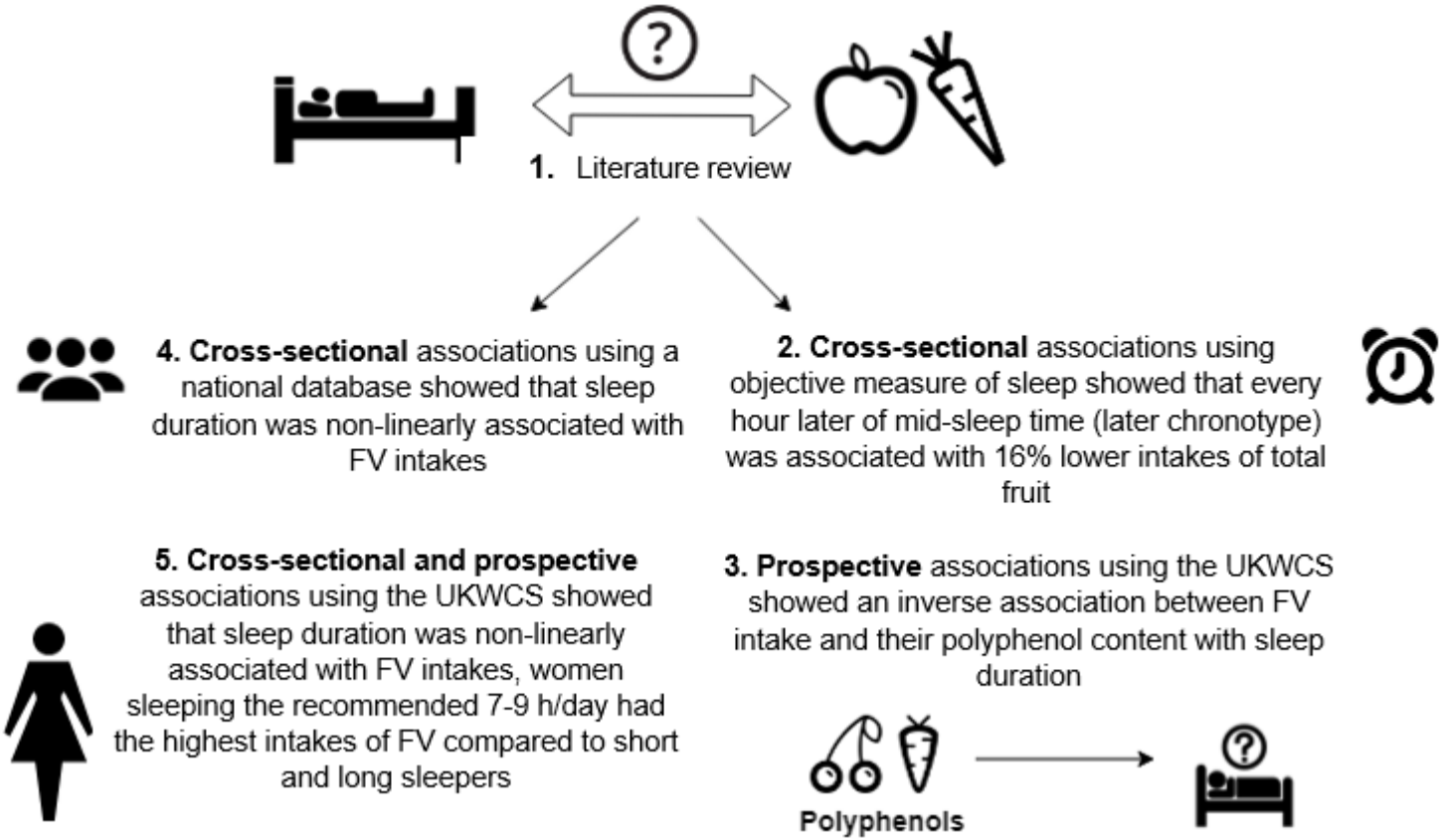


Figure 6.1. Summary of project findings.

Numbers correspond to chapters. Legend: FV (fruits and vegetables), h (hour), UKWCS (The UK Women's Cohort Study).

6.1.1 First study to assess the cross-sectional associations between objective sleep and chronotype with fruit and vegetable consumption in UK adults (Chapter 2)

Sleep disruption and FV consumption both influence disease risk and human lifespan (1-3). Studies that have assessed the associations between sleep, chronotype and diet have produced some conflicting findings (4-10). This may be partly because of the use of different methods to measure sleep, chronotype and dietary intake in different populations. Our study is the first to use objective validated methods of sleep and dietary intake in UK adults. Perhaps another reason for the discrepancy of findings is that the previous studies did not group FV items based on genus and carotenoid content as conducted in this study.

We therefore, assessed the cross-sectional associations between objective sleep, chronotype and FV consumption using a validated dietary assessment method (11) in UK adults to overcome some of the limitations of previous studies. Additionally, we used biomarkers of FV consumption unlike previous studies assessing the associations between sleep measures and FV consumption (12).

In Chapter 2, we used actimetry to measure sleep onset, offset, duration and mid-sleep time. We used the Oxford WebQ dietary assessment method that has shown good agreement with an interviewer based 24h dietary recall, the gold standard often used in nutritional epidemiology (11). We found that later chronotype was associated with lower intakes of total fruit. Borderline negative associations were shown between sleep onset and mid-sleep time with plasma vitamin C. The findings strengthen the evidence that later chronotype is associated with less healthy behaviours and provides new insights into the associations between sleep, chronotype and diet.

6.1.2 First prospective study to explore prospective associations between fruit and vegetable consumption, polyphenols and sleep duration using the large UK Women's Cohort Study dataset (Chapter 3).

After reviewing the literature, I found that there is some evidence, in small scale studies, that some fruits (13-18) and polyphenol supplementation (19, 20) may affect sleep measures. Nevertheless, nobody had studied the prospective associations between FV consumption and their polyphenol content using large cohort studies in relation to sleep duration.

Polyphenols are unstable compounds and their bioavailability and concentration differ between supplements and foods (21, 22). Therefore, in Chapter 3 I calculated the polyphenol content of 48 items of FV using the Phenol Explorer database (23) which contains data on the content of 500 polyphenols in over 400 foods from high quality articles on polyphenol composition, the impacts of food processing on the polyphenols, and metabolite composition in the body. The advantages ensured that the polyphenol content of FV applied were sensible with regard to the variety of polyphenols in each FV item. I used the UKWCS to explore the prospective associations between consumption of FV items and their polyphenol content (exposures) and sleep duration.

Whilst FV consumption may have an immediate effect on sleep duration, it may also have a longer term impact. Greenwood et al. assessed the stability of dietary patterns in women from the UKWCS using cluster analysis at baseline and after 5 years. Results showed that there was moderate stability in dietary patterns (24). Thus, exploring the longitudinal associations between FV consumption and sleep duration using the UKWCS was appropriate.

Contrary to our hypothesis, FV consumption and their polyphenol content were inversely associated with sleep duration. Although the findings were not what we anticipated, the study results are important, as they indicate the need for robust long-term intervention studies clarifying the effects of FV consumption and their polyphenol content on sleep duration and to understand the underlying mechanisms (discussed in section 6.5).

6.1.3 Use of the National Diet and Nutrition Survey to explore cross-sectional non-linear associations between sleep duration and fruit and vegetable consumption for the first time in UK adults (Chapter 4).

Short sleep duration has been identified as a risk factor for obesity (25) and cross-sectional studies reported that adults sleeping for short durations consume less healthy diets with limited information regarding effects on FV consumption (26). Furthermore, testing for non-linear associations between sleep and dietary intake has been recommended (26). However, in my literature review I found no studies that had assessed non-linear associations between sleep duration and FV consumption. We therefore used a large dataset representative of UK adults (data from years 1 to 4 of the National Diet and Nutrition Survey Rolling Programme) to explore these relationships.

In this study we observed sleep duration was non-linearly associated with FV consumption. Participants sleeping 7-8 hours/day had the highest intakes compared to

short and long sleepers. Chapter 4 strengthens the notion that people sleeping the recommended hours have a healthier lifestyle compared to short and long sleepers (27-31) and reinforces the need of non-linear exploration between sleep and diet.

After I analysed the data presented in Chapter 4, a paper was published by other researchers exploring the associations between sleep duration and dietary intake using the same dataset (32) showing no association between sleep duration and FV consumption, this may be because non-linear associations were not explored.

6.1.4 Exploring the cross-sectional and prospective non-linear associations between sleep duration and fruit and vegetable consumption using the large UK Women's Cohort Study dataset for the first time (Chapter 5).

Sleep disruption has long term effects that contribute to adverse health outcomes (33). However, do short and long sleep durations have a long-term effect on FV consumption?

We first explored the non-linear cross-sectional associations between sleep duration and FV consumption. Chapter 5 results were consistent with Chapter 4 results; sleep duration was non-linearly associated with FV consumption. Women sleeping the recommended 7-9 hours/day had the highest intakes compared to short and long sleepers. Although sleep categorisation was different between Chapter 4 and Chapter 5 due to the different sample sizes, we used a continuous variable of sleep duration to assess the non-linear associations in both Chapters and modelled this association using restricted cubic splines. Additionally, both studies assessed FV consumption using a 4-day food diary and self-report of sleep duration providing more consistency.

We also addressed this question by exploring the non-linear prospective association between sleep duration and FV consumption using the UKWCS. Interestingly, our prospective analyses with FV consumption as the outcome also confirmed the cross-sectional associations. Again, sleep duration was non-linearly associated with FV consumption with women sleeping the recommended hours having the highest intakes.

Collectively, our cross-sectional findings from Chapter 4 and Chapter 5 were consistent with the prospective analyses conducted in Chapter 5. These findings add a novel association to the literature and provide new insights to consider the non-linear association in experimental and observational studies addressing the relationship between sleep and diet.

6.2 Overall discussion

Summarising the results of this project, from cross-sectional analyses in Chapter 2, we found that later mid-sleep time was associated with lower intakes of total fruit. In Chapter 3, prospective analyses showed an inverse association between FV consumption and their polyphenol content with sleep duration (outcome). In chapters 4 and 5, cross-sectional and prospective analyses showed that sleep duration (exposure) was non-linearly associated with FV consumption with those sleeping ~7-9 hours/day having the highest intakes.

Taking the results together, it is noteworthy to say that each chapter produced a different result from the other, this could be due to the consistencies and inconsistencies across chapters that will be discussed in detail below.

6.2.1 Sleep assessment between chapters

Sleep measurements were assessed differently between the chapters. Sleep was assessed using wearable devices in Chapter 2 whereas sleep duration was self-reported in chapters 3-5. This may be one reason why no associations were evident between sleep duration and FV consumption in Chapter 2. Subjective report of sleep duration was overestimated in different populations compared to actigraphy data (34-36). Participants in chapters 3 -5 may have overestimated their sleep duration. Another inconsistency between chapters is that sleep duration in Chapter 2 was only for weekdays whereas in chapters 3-5 average sleep duration was obtained from weekdays and weekends. Sleep tends to differ between weekdays and weekends, during the weekend people typically attempt to catch up on sleep lost during weekdays resulting in longer sleep durations than weekdays (37). This was evident between chapters 2-5 since sleep duration in Chapter 2 was only for weekdays whereas chapters 3-5 included weekdays and weekend sleep duration. Mean sleep duration (objective measure) for all participants in Chapter 2 was 6.1 hours/day, mean sleep duration (subjective report) in Chapter 3 was 7.5 hours/day, mean sleep duration (subjective) for all participants in the NDNS (Chapter 4) was 7.2 hours/day and mean sleep duration (subjective) for all women from the UKWCS (Chapter 5) was 7.5 hours/day.

A positive feature in our study is the consistent methods used for sleep and dietary intake (see section 6.2.2 for dietary assessment between chapters) in chapters 4 and 5. Sleep duration was self-reported by asking two separate questions for weekdays and weekend. Self-report of sleep duration may differ by question format; participants report shorter sleep duration when asked a single question (38).

6.2.2 FV consumption assessment between chapters

Dietary assessment methods were different across studies. Chapter 2 and Chapter 3 dietary assessment methods are both FFQ. FFQs appeared in the 1960s (39) and are a widely used dietary assessment method in nutritional epidemiology however, they have shown that FFQ lack precision and often result in over-reporting, particularly for FV consumption, if each FV item is listed singly in a long list. Cross-check questions can be used to correct for misreporting of FV consumption by asking the number of servings consumed per week of FV (40) which was used in Chapter 5.

The FFQ used in Chapter 3 was validated in a subgroup of 303 women after three years of the baseline FFQ (41). Participants completed a second FFQ, a 4 day diary and gave a fasting blood sample. The FFQ and diary were coded and analysed for nutrient content. Plasma nutrient levels for iron, zinc, calcium and vitamins A, C, E and B12 were measured. Pearson correlation coefficients were highly significant ($p<0.01$) between nutrient intakes assessed by the diary and both FFQs. In addition, all nutrients (with the exception of vitamins A and E) were strongly correlated between the second FFQ and the diary compared to the baseline FFQ that was used in Chapter 3. This may be one explanation of the inverse association we found between FV items and sleep duration. Furthermore, after excluding women who had changed their diet since baseline, correlation coefficients gave similar results for the baseline FFQ. However, in Chapter 3 we did not exclude women who had changed their diet since baseline, this may be another explanation of the inverse association observed and the different results between Chapter 3 and Chapter 5 that both used the UKWCS.

A probable third explanation of the different results observed between Chapter 3 and Chapter 5 is that correlation coefficients between plasma nutrient levels and both baseline and second FFQ were statistically significant ($p <0.01$) for vitamin C (which is a biomarker of FV consumption (42) (see section 6.2.3 for biomarkers discussion)) however, the correlation was not significant for plasma vitamin C between the FFQ and diary (41). This shows that using different assessment methods give different results even if using the same participants. In Chapter 3, the FFQ was used which tends to overestimate intakes whereas in Chapter 5, food diaries were used and may underestimate intake. It is clear that both tools are measuring different aspects of diet and in this project FV consumption were measured differently between the chapters.

In Chapter 2, FV consumption was measured using the Oxford WebQ online tool which is an online FFQ that has been used by more than 200,000 participants in the UK

Biobank project. The Oxford WebQ has been validated with an interviewer-administered 24-h recall (11) and touchscreen questionnaire (43) showing good agreement between the methods. In Chapter 3, FV intake was measured using a paper FFQ and evidence show that nutrients from paper FFQ are higher than online FFQ (44).

FV consumption was measured using a 4-day food diary in both chapters 4 and 5. Training participants to fill food diaries is a main factor in providing validity and precision (45) and participants in the NDNS and UKWCS both received some training. The length of food diary administration is another factor, a minimum of 3 days is required to provide reliable information on usual food consumption. Although 7-day food diaries are commonly used, evidence show that recording periods of more than 4 consecutive days are decreased due to respondent fatigue and participants who comply differ systematically from those who don't (45). The optimal number of food records depend on the sample size of the study, the smaller the sample size, the greater the numbers of days. In both Chapter 4 and Chapter 5, we included a large number of participants and 4 consecutive days. Another factor that aids in the precision and validity of food diaries is to get a better picture of the overall diet by including both working and weekend days (45). Weekend days were over-represented in year 1 of the NDNS rolling programme and were subsequently under-sampled in year 2 to address this. On the other hand, the UKWCS participants were asked to start on a particular day (Friday, Saturday or Sunday) to control for both working and weekend days.

6.2.3 Biomarkers

A strength of our project is the use of FV biomarkers in relation to sleep measures in chapters 2, 4 and 5. In nutritional science and epidemiology, there are three main applications for biomarkers; a measure of nutritional status, validate dietary assessment instruments and as a surrogate marker of dietary intake (46). In this project, I contributed to the laboratory analyses of vitamin C biomarker to validate myfood24 in Chapter 2 and used vitamin C and carotenoid biomarkers as a surrogate marker of FV consumption in chapters 2, 4 and 5. Currently, there are three classes of dietary biomarkers: recovery, predictive, concentration and replacement. Recovery biomarkers include urinary nitrogen (for dietary protein), urinary potassium (for dietary potassium), and urinary sodium (for dietary sodium) and are used to estimate true dietary intakes. Predictive biomarkers include urinary sucrose and fructose and are predictive biomarkers of total sugar intake. Both recovery and predictive biomarkers reflect short-term intakes of

protein and sugars. Concentration and replacement biomarkers include vitamins, carotenoids, fatty acids, and phytoestrogens. These were used in chapters 2, 4 and 5.

In adjusted analyses, borderline inverse associations were found between sleep onset and mid-sleep time with plasma vitamin C in Chapter 2 whereas in Chapter 4, short sleepers had lower levels of total carotenoids and lycopene and long sleepers had higher levels of vitamin C compared with the reference group. In contrast, short sleepers had lower levels of vitamin C in Chapter 5. Using the restricted cubic spline models, Chapter 4 showed that sleep duration was non-linearly associated with plasma vitamin C, total carotenoids and lycopene with participants sleeping 7-8 hours/day having the highest levels. Similarly, the restricted cubic spline models in Chapter 5 showed a non-linear association between sleep duration, vitamin C and α-carotene. In contrast, a linear relationship was observed between sleep duration, β-carotene and lycopene. These inconsistencies may be due to the small number of participants' biomarkers in which (n=149) were measured in Chapter 5 compared to Chapter 4 (n ~ 800).

These biomarkers are based on the biomarker concentration in the specimen and have high-inter individual variability because they do not have a consistent relationship between intake and excretion. This may be one reason of the inconsistent results we found between chapters 2, 4 and 5. Therefore, concentration biomarkers cannot be used to estimate true intakes but correlate with dietary intake (47) and are used to compliment dietary assessments as used in chapters 2, 4 and 5. In Chapter 2, we didn't find a correlation between plasma vitamin C and dietary vitamin C however a positive correlation was shown between plasma β-carotene and dietary carotenoids. A plausible reason of why we didn't find correlation between dietary vitamin C and plasma vitamin C is that the strength of correlation may be influenced by the sample size (48).

The inconsistent results may be due to several factors; bioavailability, metabolism nutrient-nutrient interaction excretion, sampling, storage and analytical techniques. It has been estimated that the annual loss of vitamin C in plasma during long storage periods was between 0.3 and 2.4 µmol/L (46). Storage periods of biomarker samples were different between chapters 2, 4 and 5. Furthermore, the use of different analytical methods may be one reason of the different results between the chapters (46). In chapters 2, 4 and 5, plasma carotenoids were analysed using HPLC. Plasma vitamin C was also analysed by HPLC in Chapter 2 (Appendix B (B.3.)) and Chapter 5 whereas the NDNS (Chapter 4) used fluorometric assay (49). HPLC is used to separate, identify and quantify each component in a mixture. A pressurized liquid solvent containing the

sample mixture is pumped to a column filled with solid adsorbent – the adhesion of molecules to a surface- material. The components are separated due to the different interaction with the adsorbent material causing different flow rates as they flow out of the column (50). Fluorometric assays provide a sensitive fluorescent for quantifying the required content e.g. total ascorbic acid in cell lysate (51). Another factor to consider is that the relationship between intake and absorption is linear for vitamin C only for intakes below ~100mg/day and intakes above 120 mg/day reach a plateau. Since vitamin C is a water-soluble vitamin, renal excretion is minimised for lower plasma vitamin C concentrations thus affecting biomarker concentration (47).

Carotenoids are lipid-soluble therefore their bioavailability are largely determined by their lipophilicity therefore, their absorption are affected by the fat content in the food matrix. However, since they are not under homeostatic control, blood carotenoid levels are sensitive to intake but are influenced by several factors. The first factor is body weight, intervention studies found that the correlation between carotenoid intakes and blood concentrations were stronger in normal weight individuals than in obese (46). The second factor that may influence blood carotenoid levels, is lower levels of vitamin A status because some carotenoids can be metabolised to retinol however, this was not measured in this project. Third factor is supplement intake of β-carotene, lower blood levels of carotenoids may result from the competition between carotenoids given as supplements. Therefore, as sensitivity analyses, we excluded supplement users in chapters 3, 4 and 5 and not in Chapter 2 due to the small sample size. The last factor that may resulted in distinctive results is the use of two different dietary assessment methods; the FFQ and food diaries. In a meta-analyses of 26 studies, FFQ and dietary recalls food diaries were moderately associated with plasma vitamin C and were affected by body size, smoking, use of supplements, food processing techniques and disease status (42). We tried overcoming these limitations by adjusting for smoking and BMI and excluding participants using supplements and those with a chronic disease in sensitivity analyses.

Furthermore, in a sub-sample of 54 women from the UKWCS, it was found that plasma ascorbic acid and β-carotene were good indicators of vitamin C and β-carotene intake when using 4-day food diaries and less marked when assessed by the 24-h recall (52). The study concluded that the practice of using plasma ascorbic acid and β-carotene biomarkers as a proxy measure of dietary intake is not valid and that they are not a reflection of only dietary intake but also a number of physiological processes.

Collectively, concentration biomarkers reflect long-term intakes of FV. Future dietary intervention studies with increased FV consumption should measure a combination of plasma vitamin C, carotenoids and polyphenols to validate candidate biomarkers and establish a correlation.

6.2.4 Cofounders

One of the possible reasons of epidemiological studies providing contradictory findings is the difference in confounder adjustment (26). A positive feature in our study is the consistent adjustment for confounders identified using the directed acyclic graph (Appendix B (B.4.)). In chapters 2 and 4 we adjusted for age, sex, SES, ethnicity, smoking and total energy intake. In chapters 3 and 5 we adjusted for the same variables with the exception of sex because only women were included in the analyses.

In chapters 3 and 5, we used the UKWCS to assess the association between sleep duration and FV consumption. Pollard et al investigated the lifestyle factors affecting FV consumption of women from the UKWCS. The strongest predictors of higher reported levels of FV consumption were being vegetarian/ vegan, taking vitamins or supplements, being married, educated to A-level and higher SES (53). Furthermore, Pollard et al, explored the motivations for FV consumption in a sub-sample from the UKWCS using The Food Choice Questionnaire. Health and natural content were the main motivating factors for FV consumption (54). Although the previous studies identified an association between income, SES and sleep measures, price was not seen as a prime motivating factor in Pollard et al study reflecting the high socio-economic group of women from the UKWCS. However, price and SES are main influencers on FV consumption and it was previously shown that lower socioeconomic groups consume less FV than those in higher socioeconomic groups (55). Therefore, SES was controlled for in all analyses in this project.

Personality measures contain five traits of personality existing in different combinations within each individual. These traits include neuroticism, extraversion, openness to experience, agreeableness and conscientiousness (56). Individuals who score high in neuroticism are more emotionally unstable and have higher levels of anxiety and depression. Extraversion trait is described by preference for social interaction, predisposition to positive emotions, activity, warmth and excitement-seeking. Openness to experience trait is described by active imagination, aesthetic sensitivity, attentiveness to inner feelings, variety and curiosity. Agreeableness trait is described by trust, concern for others and cooperation. Conscientiousness trait is described by organization,

persistence, self-discipline, ambition and a need for achievement. Higher extraversion, agreeableness and conscientiousness were associated with better sleep whereas higher neuroticism was associated with poor sleep in two population based samples from Australia and Finland (57). Similarly, in a cross-sectional study of 1,406 Korean women, conscientiousness was the most noteworthy predictor of sleep quality measured by PSQI. Women high in conscientiousness were least likely to have poor sleep quality and high neuroticism was associated with poor sleep quality (58). This was also evident in 436 university students (59). The previous studies showed that sleep is influenced by personality traits which were not considered in this study due to the unavailability of the data. These confounders should be considered in future studies.

Sleep is a learned behaviour from early childhood. Parental behaviours at bedtime and to their child's nocturnal awakening's play a major role in consolidating their child's sleep patterns. In a representative sample of Canadian infants (n=1741), feeding the child after an awakening at 5 months of age was the strongest factor associated with not sleeping 6 consecutive hours per night. In addition, at 17 months and 29 months of age, parental presence until sleep onset was the strongest factor associated with not sleeping 6 consecutive hours at night (60). This study shows that parental behaviours is associated the child's sleep patterns. However, sleep needs differ by age and the recommended amount of sleep ranges from 9-17 hours per day in children, 8-10 hours/day in adolescents and 7-9 hours in adults and older adults (61). The role of learnt sleeping habits during childhood on adulthood sleep is unknown and there is a need of studies to assess this association.

6.2.5 Studies supporting the inversed U-shaped association between sleep duration and FV consumption

In Chapter 4 and Chapter 5, both short and long sleepers consumed less FV compared to those sleeping ~7-9 hours/day. One explanation of these results may be the behaviour and characteristics of short and long sleepers; which have been studied since the 1970s. Webb reported that adolescents sleeping ≤ 6.5 hours had no difference in sleep stages compared to controls whereas long sleepers (≥ 8.5 hours) obtained more REM sleep (62). In contrast to a further study by Webb, short sleepers (≤ 5.5 hours) had less REM sleep compared to controls (63). The different results between Webb's studies may be due to the dissimilar definition of short and long sleep. In a more recent study, long sleep durations were not explained by differences in comorbidity or sleep disorders and showed that long sleepers spent more time in bed compared to normal sleepers (64).

However, other researchers suggested that long sleep may be a proxy for poor health or mortality (65). Patel et al focused on characteristics of long sleepers in adults and identified factors that could potentially explain the association between long sleep and mortality. Depression and low SES were the strongest – as confounders or as causal-influencers for the long sleep duration and mortality association (66). Rayward et al clustered physical activity, sleep duration and sleep quality and found that clusters with poor behaviours were associated with poor health status (67). A combination of several unhealthy lifestyle factors (smoking, BMI >25, high alcohol consumption, no exercise and unfavourable eating patterns) were associated with higher odds of non-restorative sleep compared to participants with a healthy lifestyle (68).

In Chapter 4 and Chapter 5, we found an inverse U-shaped association between sleep duration and FV consumption with those sleeping the recommended ~7-9 hours/day having the highest intakes. This association may be supported by the U-shaped association found in other studies between sleep disruption and unfavourable behaviours and characteristics. In a representative sample of US adults, sleep complaints were associated with sleep duration in a U-shaped relationship. Short sleepers and long sleepers reported sleep problems and those sleeping 7-8 hours reporting it less frequently (29). Other characteristics including smoking, alcohol drinking and physical inactivity were associated with short and long sleep durations (27, 28). This was also shown in Sweden women with short and long sleepers being physically inactive, smokers, physiologically distressed and increased waist circumference compared to normal sleepers (30). Both short and long sleep duration were negatively associated with education level, family income, and leisure-time physical activity in Chinese women (31) and a large Chinese adult population (69). In Japanese adults, the U-shaped association between sleep duration and health were explained by the U-shaped association between sleep duration and disrupted sleep with psychosocial stress from work and family life. Short sleep duration was associated with long work hours and high work-family conflict whereas long sleep was associated with daily alcohol drinking. Participants sleeping ~8 hours had the lowest prevalence of poor sleep and unfavourable behaviours and characteristics (70). Interestingly, the U-shaped association was found between sleep duration and serum lipid profiles in Chinese women (71), between sleep duration and diabetic retinopathy (72) and sleep duration and the risk of falls (73).

Other studies only found an association between short sleep duration and less healthy behaviours. Insufficient sleep in 323,047 US adults was associated with unemployment,

decreased age, income, education, physical activity; worse diet and overall health; and increased household size, alcohol, and smoking (74). Lower SES was associated with shorter sleep duration in US adults (75). In ~ 30,000 Japanese adults, lack of exercise, poor health status and irregular eating habits were associated with insufficient sleep (76). Odds of short sleep increased for the lowest household income and lower education in adults followed for 34 years (77). Similarly, living in urban areas, smoking, lower level of education and alcohol consumption were associated with lower odds of having adequate and quality sleep in Canadian women (78). Therefore, it is important to identify the individual, social and environmental determinants of sleep among adults (79).

Overall, the inverse U-shaped associations observed in the previous studies may explain our findings of the inverse U-shaped association between sleep duration and FV consumption. A nutritious diet including high intakes of FV are considered one of the main keys to a healthy lifestyle (80). Therefore, the previous studies showed that sleeping the recommended hours are associated with a healthier lifestyle supporting our findings of higher intakes of FV in participants sleeping ~7-9 hours/day. This project may be part of the complex puzzle of the U-shaped association between sleep measures, morbidity and mortality. Future research exploring whether FV consumption acts as a mediator between sleep disruption, morbidity and morbidity are necessary to clarify the underlying mechanisms.

In this project, it is important to note that the assessment methods used for sleep and FV consumption (see sections 6.2.1 and 6.2.2) may have a role in providing conflicting results. This was shown between Chapter 3 and Chapter 5 that used the UKWCS. We used biomarkers of FV to compliment the dietary assessment tools however, biomarkers are influenced by several factors that were not considered in this study (see section 6.2.3). In addition, sleep and diet are complex measures and are affected by numerous aspects that could have impacted our results (see section 6.2.4). We used sleep as an exposure in chapters 2, 4 and 5 in contrast to Chapter 3 that was used as an outcome due to the reciprocal associations observed in the literature (see section 1.5). Future epidemiological studies should consider this and may assess the associations in both directions and experimental studies will clarify the significant effects of each direction (see section 6.5). In summary, this project have identified novel associations between sleep duration and FV consumption.

6.3 Implications of our findings

With the reciprocal relationship between sleep and diet in mind, our findings have two main implications that may contribute to public health. Healthy lifestyle patterns have focused mainly on dietary intake and physical activity however, recently, awareness of sleep as a healthy behaviour has been raised (81, 82). A first implication, dietary guidelines could include information on sleep and chronotype. A natural starting point is improving sleep hygiene by recommending behavioural and environmental practices to promote better sleep. These practices include optimising temperature, removing light, bedding, mattresses and sound. Sleep hygiene education have shown effective enhancement of sleep quality and decreased daytime sleepiness in adults (83, 84) and children (85, 86). Dietary guidelines and nutrition professionals could promote better sleep by eliminating or reducing caffeinated foods, and beverages before bedtime, smoking cessation, massage therapy, dim or reduce bright lights during dark hours, engage in physical activity throughout the day and have consistent sleeping and waking times (87).

If future studies continue to support previous findings that later chronotype initiates lower consumption of FV and less healthy behaviours, governments should revise their guidelines accordingly. Dietary recommendations tailored to late chronotypes would ultimately be another worthwhile development. Such recommendations may include pre planning and preparation of meals to prioritise and increase the consumption of FV. Furthermore, if future studies support that the timing of FV consumption may impact sleep duration, quality and timing, recommendations on the optimal time of FV consumption alongside the 5-a-day guidelines (88) will be informative. However, as few human studies have addressed these questions, a greater body of evidence would be required before such recommendations could be proposed.

Promoting FV consumption is a key objective of food and nutrition policy interventions conducted by governments and non-governments. The success of campaigns and interventions conducted around the world in terms of increasing the daily consumption of FV remain modest (89). The second implication of this work is the incorporation of sleep screening in GP practices, hospitals, weight-loss programs, and campaigns targeting higher consumption of FV. Sleep screening questions on timing, duration, difficulty falling asleep, waking up at night, refreshed feeling upon waking and sleepiness during the day should be included (87). If desired answers are not received, further

assessment can be conducted by using the PSQI. Participants with an indication of poor sleep or sleep disorders should be referred to sleep clinicians.

6.4 Project limitations and strengths

An unavoidable consequence of using data collected by other groups (like the NDNS, UKWCS and myfood24 validation study) is inconsistency. A limitation of this project is some inconsistencies in methods between chapters. Sleep was assessed using wearable devices in Chapter 2, questionnaires in chapters 3 and 5 and a computer-assisted personal interview programme in Chapter 4. Similarly, diet was assessed using different methods in these chapters (discussed in detail in section 6.2).

The cross-sectional nature in chapters 2, 4 and 5 may include the possibility of reverse causality. We found that short and long sleep durations are associated with lower intakes of FV however, it could be that those consuming less FV accompanied with other unhealthy behaviours may influence sleep duration. Other limitations of epidemiological methods include undetected bias and incomplete adjustment for confounding, measurement error in the exposure estimate, and other biases in participant selection or data collection. In particular, models applied here do not adjust for environmental factors such as light exposure, the location of habitation and deprivation scores, or additionally for other dietary components associated with sleep such as protein intake which may contribute to residual confounding. Significant results due to multiple testing is also a possibility due to the extensive amount of analyses. However, this is a necessary approach if associations between FV items and sleep duration are to be elucidated. Therefore, where appropriate, narrow confidence intervals (99% CI) were adapted in multiple chapters to reduce false positives. The reciprocal associations between sleep and diet have been more identified in sex-stratified groups (26). In a meta-analysis including ~ 15,000 participants from 9 US and European cohort studies found that short sleep was associated with higher carbohydrate intake in women only (90). Another limitation of this project is the inclusion of only women in chapters 3 and 5, the associations observed may be different in men (91-93). However, chapters 2 and 4 included both men and women representative of the UK population and we adjusted for sex in all analyses to overcome this limitation.

Previous results from randomised trials indicate that the effects of specific nutrients on diseases are small (94). For this reason, some researchers have used randomised trials of dietary patterns instead of single nutrients, this may overcome some of the limitations (95). I acknowledge that my research is not immune to the limitations of using FV intakes

individually and not dietary patterns. However, dietary patterns have been stable for 5 years in women from the UKWCS (24) and in other studies (96-99). Therefore, choosing FV individually was a reasonable approach. Additionally, in Chapter 4, the disaggregation of foods containing FV into their components helped in giving better estimates of FV intakes (100). This also may have overcome some of the limitations of studying specific foods and not dietary patterns. My intention with this project was to maximise my contribution to the literature within the constraints of the resources available.

This project has several strengths. First, this project included a large sample size in chapters 3, 4 and 5. Second, the consistency in sleep and dietary assessment methods in chapters 4 and 5 is another strength. Third, to our knowledge, this is the first study that has extensively studied the prospective associations between sleep duration and FV consumption and explored the associations between FV items by polyphenol content on sleep duration. Fourth, using Phenol Explorer as a reference database for calculating the polyphenol content of FV has certain advantages. This is because extensive methods were implemented to collect high-quality literature articles on polyphenol composition, the impact of food processing on polyphenols and metabolite composition in the body, which ensured that the polyphenol content applied here were sensible with regard to the variety of polyphenols in FV items. Fifth, analyses were conducted in three UK populations and comparison between them may provide a bigger picture of the association between sleep duration and FV consumption. Finally, this is the first study to explore the non-linear associations, both cross-sectional and prospective, between sleep duration and FV consumption.

6.5 Possible directions for future work

Beginning with Chapter 2, it would be productive to reach agreement on the best ways to assess sleep duration and chronotype. Although the recommendations for sleep duration have been provided (61), individual differences need to be considered by exploring optimal sleep duration in a laboratory. Next, the difference between optimal sleep duration and habitual sleep duration can be obtained, this difference represents potential sleep loss which is not clearly recognized to individuals. Previous findings confirmed that evaluating optimal sleep duration may be a useful clinical marker of sleep loss and individual differences (101). However, laboratory experiments of sleep deprivation have shown that individuals have differential neurobehavioral vulnerability to sleep loss suggesting a polygenetic phenotype (102, 103). Omics (transcriptomics,

epigenomics, and metabolomics) approaches were suggested as biomarkers for identifying differential vulnerability to sleep loss (104). Identification of such markers will provide a viable means to determine those individuals who may need more habitual sleep or who may need to prevent or mitigate sleep deprivation through lifestyle choices and effective interventions and countermeasures (e.g., caffeine, naps, etc.). Variation in sleep measures and chronotype are related to circadian clock genes and non-circadian genes (105). Sleep and diet research may need to explore the effects of sleep disruption on FV consumption based on genetic disparities.

Chapter 3 focused on FV items and their polyphenol content with sleep duration. It would be informative to explore the effects on other sleep measures (sleep timing and quality). Furthermore, future intervention studies comparing the effects of different FV items (individually and combined) on sleep measures will be instructive and may be beneficial in identifying the underlying mechanisms. Previous studies found that activities done during the day have an effect on sleep (106-110). Related to this, given the lack of dietary timing data, we did not consider the time of FV consumption. An example is comparing the effects of FV consumption at specified time points on sleep measures. Nevertheless, little is currently known about associations between many FV items and sleep measures.

Adherence to a Mediterranean diet (the highest tertile) was associated with better sleep quality compared to those in the lowest tertile (111). It could be that different FV items may have different effects on sleep measures due to their moisture, water content (112), fibre, polyphenols and antioxidants (113). Lower consumption of dietary fibre was associated with less SWS (114, 115) however, few studies explored the effects of different polyphenols on sleep architecture (see section 1.8.3.2.) and more studies will be instructive. People who eat several servings of FV per day, their total polyphenol intake reaches ~1 g/d (116). The assessment of polyphenol intake is difficult to evaluate by using similar methods to dietary assessment due to their bioavailability and bio-efficacy variances (21). Therefore, biomarkers for polyphenol exposure would be very useful. Limited studies found that food matrix effects on the bioavailability of polyphenols and thus affecting their absorption. Future studies may compare the effects of different polyphenols on sleep measures between fasting participants and participants consuming a complex meal or FV items. Consideration of the dietary fibre content of FV items in these studies are necessary because dietary fibre stimulates intestinal fermentation that may influence the production of microbial metabolites that may have consequences on the absorption of polyphenols (116). Another factor to consider in studies exploring the

effects of polyphenols from FV on sleep, is controlling for other sources of high polyphenol content from foods such as coffee, tea, red wine, soy and chocolate.

The antioxidant properties of polyphenols have been widely studied (117). However, it is uncertain whether increased antioxidant nutrient intake or supplementation would modify sleep. Nonetheless, studies reported reduced antioxidant capacity in serum of patients with obstructive sleep apnoea (OSA) (118), and reduced dietary intake of antioxidants in veterans with OSA (119). Related to OSA, participants with the metabolic syndrome had reduced serum concentrations of antioxidants (120). Furthermore, antioxidant nutrient intake from high consumption of FV or supplement intake were proposed as potential moderators of cognitive decline and CVD from OSA (121). In a recent cross-sectional study conducted among 3,941 Korean men, short sleepers (<6 hours) with low consumption of dietary antioxidant had a higher risk of obesity than those with a high consumption of dietary antioxidants (122). These results suggest that the increased risk of obesity associated with short sleep duration may be modified by the consumption of dietary antioxidants. In light of this, as a starting point, epidemiological studies could subgroup FV based on similarity of total antioxidant capacity to explore their relationship with sleep. Ten subgroups of FV were proposed based on food component and classification variables (botanic family, plant part, colour and total antioxidant capacity) (123). Furthermore, long- term prospective randomised controlled clinical trials can study the effects of antioxidants from FV combined based on the 10 groups, or antioxidants from supplements in individuals with short, recommended and long sleep duration. In addition, other sleep measures (sleep architecture, quality and timing) could be explored in relation to antioxidant intake. Objective markers of antioxidant intake and oxidative stress should be initiated and compared across persons with short, recommended and long sleep durations, and also compared across persons with poor/good sleep quality and those with different chronotypes. In those randomised controlled trials, it is necessary to select FV that undertaken similar food processing and handling methods to overcome their effects on preservation of antioxidants (124).

Relevant to both Chapter 4 and Chapter 5, sleep restriction studies (see section 1.6.2) provide conflicting results on their effects on FV consumption and there are a lack of studies assessing the timing of sleep in relation to FV consumption, more studies investigating the timing of sleep and taking into account chronotype are required to clarify this relationship. Studies exploring the effects of sleep extension on FV consumption (see Table 1.3) are few, more studies are needed to help clarify the underlying

mechanisms between sleep disruption and FV consumption. Non-linear relationships between FV and sleep need to be considered in sleep restriction/extension studies. A recent study showed the feasibility of extending sleep by sleep hygiene intervention and their effects on dietary intake and energy balance (125). The results showed that sleep extension led to reduced intakes of free sugars compared to controls. It would be interesting to conduct a similar study and explore the effects of sleep extension in habitual short sleepers on FV consumption. One factor that may influence the effects of sleep extension interventions on diet is chronotype. Therefore, comparing the effects of sleep restriction/extension on FV consumption between different chronotypes is essential.

Additional studies of effects of sleep restriction/extension on FV consumption in different populations would also be useful. Differences in sleep between different races and ethnicities have been reported. Black individuals tend to have shorter sleep durations and poorer sleep quality than white individuals (126-129). It has been proposed that the underlying mechanisms of ethnic/racial disparities in sleep include several potential biological, psychobehavioral, sociocultural and environmental factors (128, 129). These potential mediators are important to explore in future research conducted in different race/ethnic individuals assessing associations between sleep measures and FV consumption. A strength of this project is that we adjusted for ethnicity in all chapters of analyses. Other populations to consider for example; elderly people, clinical populations, shift workers and less- developed countries. Little is known about sleep and FV consumption in these people, to my knowledge.

A study explored the effects of short and long sleep durations on taste preference in healthy adults. Habitual long-sleepers preferred sweeter stimuli following sleep restriction while sleep extension did not change taste preference in habitual short-sleepers (130). However, in adolescents, sweet foods were more appealing after sleep restriction (131). This may be an explanation for the low intakes of FV in short and long sleepers in our study. Because FV require some preparation, convenience and time are important factors today as the pace of life has increased, therefore, people tend to buy easy to prepare products (89). In light of this, the question of whether short and long sleepers substitute FV with off the shelf and convenient desserts and sweets is not well understood and will be a valuable point of inquiry to address in future studies that assess the association between sleep measures and FV consumption.

Reciprocity between sleep and exercise exists; sleep disruption could impair an individual's capacity for exercise and increase the risk of exercise-induced injuries, conversely, acute and regular exercise effect sleep architecture and measures depending by numerous factors; sex, age, fitness level, BMI, intensity and duration of exercise, time of day and environment (indoor or outdoor). The results are conflicting and effects of exercise on sleep were mostly shown in people with sleep disorders and trivial improvement in sleep in individuals with good sleep. (87, 132). There is not enough evidence that exercise may effect FV consumption, therefore we did not adjust for it in this project in our main analyses. As there is a paucity of human studies on this subject, it is important to study how to optimise exercise protocols to increase FV consumption and improve sleep.

Studying the complex relationship between sleep and diet needs to take into consideration numerous components. Current usage of digital devices is unprecedented and keeping pace with the digital revolution we are experiencing is fundamental. Future sleep extension studies need to compare between the effects of digital cognitive behavioural therapy (133) and sleep hygiene education on sleep, quality of life and psychological well-being. Another factor to consider in future studies is stress. Mental stress and depression have increased dramatically over the last 50 years. Stress has been found to be associated with disrupted sleep, increase in reward palatable food thus causing obesity. On the other hand, improving sleep patterns and nutritional status may reduce the severity of stress and mental disorders (134). This highlights the importance of the need to further examine the complex relationship between sleep, diet and stress. Related to this, sleep and self-control are intertwined, sleep disrupted individuals are at an increased risk of impaired decision making including dietary selection (135). Self-control has two effects on health behaviour (such as physical activity, eating healthily (high intakes of FV for example), reducing alcohol intake and not smoking); an indirect effect mediated by intentions and a moderated effect on the intention- health behaviour relationship. Hagger et al. proposed several pathways of how sleep may affect health behaviour in the context of the health self-control model (136). People with better sleep quality and sufficient duration will be more likely to be able to form intentions to engage in health behaviours. The underlying mechanism for this effect is because better sleep (quality and quantity) provide individuals with sufficient cognitive resources for more effective planning. In light of this, does self-control have a role in the association between sleep duration and FV consumption? Future studies addressing this will be extremely valuable in clarifying the underlying mechanisms.

Based on health psychology research from five decades, a nutritious diet and sleep moderation and optimism are two of the main keys to a long, happy, healthy and productive life (80). This project showed that sleeping the recommended hours of sleep is associated with higher intakes of FV.

6.6 Conclusions

The substantial attribution of sleep disruption and low intakes of FV on the global burden of diseases are well documented and understanding the reciprocal relationship between them is necessary.

In this project we explored the associations between sleep duration and FV consumption in three UK adult populations. The first part of this project explored the cross-sectional associations between objective measures of sleep and chronotype with FV consumption. Later chronotype was associated with lower intakes of total fruit. This finding may help in developing dietary guidelines for people with different chronotypes. Next, using the large UKWCS, prospective analyses showed an inverse association between FV items and their polyphenol content with sleep duration. The study provided insight for future research to explore the timing of FV consumption which was not measured in our study. We then focused on sleep duration as the exposure, using a representative sample of UK adults, finding a non-linear cross-sectional association between sleep duration and FV consumption with short and long sleepers consuming less FV. Finally, consistent with previous, using the UKWCS, non-linear associations were observed from cross-sectional and prospective analyses with women sleeping the recommended 7-9 hours/day having the highest intakes of FV. These findings show the necessity of exploring non-linear associations between sleep and diet and pave the way for studies of whether this association is related to the relationship between sleep disruption, morbidity and mortality.

References of Chapter 6

1. Itani O, Jike M, Watanabe N, et al. Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression. *Sleep Medicine*, 2017, **32**, pp.246-256.

2. Jike M, Itani O, Watanabe N, et al. Long sleep duration and health outcomes: A systematic review, meta-analysis and meta-regression. *Sleep Medicine Reviews*, 2018, **39**, pp.25-36.

3. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies. *International Journal of Epidemiology*, 2017, **46**(3), pp.1029-1056.

4. Patterson F, Malone SK, Lozano A, et al. Smoking, Screen-Based Sedentary Behavior, and Diet Associated with Habitual Sleep Duration and Chronotype: Data from the UK Biobank. *Annals of Behavioral Medicine*, 2016, **50**(5), pp.715-726.

5. Arora T and Taheri S. Associations among late chronotype, body mass index and dietary behaviors in young adolescents. *International Journal of Obesity (2005)*, 2015, **39**(1), pp.39-44.

6. Malone SK, Zemel B, Compher C, et al. Characteristics Associated with Sleep Duration, Chronotype, and Social Jet Lag in Adolescents. *Journal of School Nursing*, 2016, **32**(2), pp.120-31.

7. Patterson F, Malone SK, Grandner MA, et al. Interactive effects of sleep duration and morning/evening preference on cardiovascular risk factors. *European Journal of Public Health*, 2018, **28**(1), pp.155-161.

8. Sato-Mito N, Sasaki S, Murakami K, et al. The midpoint of sleep is associated with dietary intake and dietary behavior among young Japanese women. *Sleep Medicine*, 2011, **12**(3), pp.289-94.

9. Sato-Mito N, Shibata S, Sasaki S, et al. Dietary intake is associated with human chronotype as assessed by both morningness-eveningness score and preferred midpoint of sleep in young Japanese women. *International Journal of Food Sciences and Nutrition*, 2011, **62**(5), pp.525-32.

10. Yoshizaki T, Komatsu T, Tada Y, et al. Association of habitual dietary intake with morningness-eveningness and rotating shift work in Japanese female nurses. *Chronobiology International*, 2018, **35**(3), pp.392-404.

11. Liu B, Young H, Crowe FL, et al. Development and evaluation of the Oxford WebQ, a low-cost, web-based method for assessment of previous 24 h dietary intakes in large-scale prospective studies. *Public Health Nutrition*, 2011, **14**(11), pp.1998-2005.

12. Duke CH, Williamson JA, Snook KR, et al. Association Between Fruit and Vegetable Consumption and Sleep Quantity in Pregnant Women. *Maternal and Child Health Journal*, 2017, **21**(5), pp.966-973.

13. Garrido M, González-Gómez D, Lozano M, et al. A jerte valley cherry product provides beneficial effects on sleep quality. Influence on aging. *The Journal of Nutrition, Health & Aging*, 2013, **17**(6), pp.553-60.

14. Garrido M, Espino J, González-Gómez D, et al. A nutraceutical product based on Jerte Valley cherries improves sleep and augments the antioxidant status in humans. *e-*

SPEN, the European E-Journal of Clinical Nutrition and Metabolism, 2009, **4**(6), pp.e321-e323.

15. Garrido M, Paredes SD, Cubero J, et al. Jerte Valley cherry-enriched diets improve nocturnal rest and increase 6-sulfatoxymelatonin and total antioxidant capacity in the urine of middle-aged and elderly humans. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 2010, **65**(9), pp.909-14.

16. Lin H, Tsai P, Fang S, et al. Effect of kiwifruit consumption on sleep quality in adults with sleep problems. *Asia Pacific Journal of Clinical Nutrition*, 2011, **20**(2), pp.169-74.

17. Pigeon W, Carr M, Gorman C, et al. Effects of a Tart Cherry Juice Beverage on the Sleep of Older Adults with Insomnia: A Pilot Study. *Journal of Medicinal Food*, 2010, **13**(3), pp.579-583.

18. Howatson G, Bell PG, Tallent J, et al. Effect of tart cherry juice (Prunus cerasus) on melatonin levels and enhanced sleep quality. *European Journal of Nutrition*, 2012, **51**(8), pp.909-16.

19. Romain C, Alcaraz PE, Chung LH, et al. Regular consumption of HolisFiit, a polyphenol-rich extract-based food supplement, improves mind and body well-being of overweight and slightly obese volunteers: a randomized, double-blind, parallel trial. *International Journal of Food Sciences and Nutrition*, 2017, **68**(7), pp.840-848.

20. Uddin M, Biswas D, Ghosh A, et al. Consumption of Fruitflow® lowers blood pressure in pre-hypertensive males: a randomised, placebo controlled, double blind, cross-over study. *International Journal of Food Sciences and Nutrition*, 2018, **69**(4), pp.494-502.

21. Manach C, Williamson G, Morand C, et al. Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies. *The American Journal of Clinical Nutrition*, 2005, **81**(1 Suppl), pp.230S-242S.

22. Martin K and Appel C. Polyphenols as dietary supplements: A double-edged sword. *Nutrition & Dietetics*, 2009.

23. Neveu V, Perez-Jimenez J, Vos F, et al. Phenol-Explorer: an online comprehensive database on polyphenol contents in foods. *Database: The Journal of Biological Databases and Curation*, 2010, **2010**, p.bap024.

24. Greenwood D, Gilthorpe M, Golding C, et al. Stability over time of dietary patterns in the UK Women's Cohort Study. *Proceedings of the Nutrition Society*, 2003 **62**, p.89A.

25. Cappuccio FP, Taggart FM, Kandala NB, et al. Meta-Analysis of Short Sleep Duration and Obesity in Children and Adults. *Sleep*, 2008, **31**(5), pp.619-26.

26. Dashti HS, Scheer FA, Jacques PF, et al. Short sleep duration and dietary intake: epidemiologic evidence, mechanisms, and health implications. *Advances in Nutrition*, 2015, **6**(6), pp.648-59.

27. Bixler E. Sleep and society: an epidemiological perspective. *Sleep Medicine*, 2009, **10 Suppl 1**, pp.S3-6.

28. Magee CA, Iverson DC and Caputi P. Factors associated with short and long sleep. *Preventive Medicine*, 2009, **49**(6), pp.461-7.

29. Grandner M and Kripke D. Self-reported sleep complaints with long and short sleep: A nationally representative sample. *Psychosomatic Medicine*, 2004, **66**(2), pp.239-41.

30. Theorell-Haglow J, Berglund L, Janson C, et al. Sleep duration and central obesity in women - differences between short sleepers and long sleepers. *Sleep Medicine*, 2012, **13**(8), pp.1079-85.

31. Tu X, Cai H, Gao YT, et al. Sleep duration and its correlates in middle-aged and elderly Chinese women: the Shanghai Women's Health Study. *Sleep Medicine*, 2012, **13**(9), pp.1138-45.

32. Potter GDM, Cade JE and Hardie LJ. Longer sleep is associated with lower BMI and favorable metabolic profiles in UK adults: Findings from the National Diet and Nutrition Survey. *PloS One*, 2017, **12**(7), p.e0182195.

33. Frank S, Gonzalez K, Lee-Ang L, et al. Diet and Sleep Physiology: Public Health and Clinical Implications. *Frontiers in Neurology*, 2017, **8**, p.393.

34. Jungquist CR, Pender JJ, Klingman KJ, et al. Validation of Capturing Sleep Diary Data via a Wrist-Worn Device. *Sleep Disord*, 2015, **2015**, p.758937.

35. Tonetti L, Mingozzi R and Natale V. Comparison between paper and electronic sleep diary. *Biological Rhythm Research*, 2016, **47**(5), pp.743-753.

36. Lauderdale DS, Knutson KL, Yan LL, et al. Self-reported and measured sleep duration: how similar are they? *Epidemiology*, 2008, **19**(6), pp.838-45.

37. Wittmann M, Dinich J, Merrow M, et al. Social jetlag: Misalignment of biological and social time. *Chronobiology International*, 2006, **23**(1-2), pp.497-509.

38. Lauderdale DS. Survey Questions About Sleep Duration: Does Asking Separately About Weekdays and Weekends Matter? *Behavioral Sleep Medicine*, 2014, **12**(2), pp.158-168.

39. Hankin JH, Reynolds WE and Margen S. A short dietary method for epidemiologic studies. II. Variability of measured nutrition intakes. *The American Journal of Clinical Nutrition*, 1967, **20**(9), pp.935-45.

40. Cade J, Thompson R, Burley V, et al. Development, validation and utilisation of food-frequency questionnaires - a review. *Public Health Nutrition*, 2002, **5**(4), pp.567-87.

41. Spence M, Cade JE, Burley VJ, et al. Ability of the UK Women's Cohort Study food frequency questionnaire to rank dietary intakes. *Proc Nut Soc*, 2002, **61**, p.117A.

42. Dehghan M, Akhtar-Danesh N, Mcmillan CR, et al. Is plasma vitamin C an appropriate biomarker of vitamin C intake? A systematic review and meta-analysis. *Nutrition Journal*, 2007, **6**, p.41.

43. Bradbury KE, Young HJ, Guo W, et al. Dietary assessment in UK Biobank: an evaluation of the performance of the touchscreen dietary questionnaire. *Journal of Nutritional Science*, 2018, **7**, p.e6.

44. Carrascosa RG, Segovia PG and Monzo JM. Paper and pencil vs online self-administered food frequency questionnaire (FFQ) applied to university population: a pilot study. *Nutricion Hospitalaria*, 2011, **26**(6), pp.1378-1384.

45. Ortega RM, Perez-Rodrigo C and Lopez-Sobaler AM. Dietary assessment methods: dietary records. *Nutricion Hospitalaria*, 2015, **31**, pp.38-45.

46. Lovegrove J, Hodson L, Sharma S, et al. *Nutrition research methodologies.* The Nutrition Society textbook series. Chichester, West Sussex: Wiley Blackwell,, 2015.

47. Jenab M, Slimani N, Bictash M, et al. Biomarkers in nutritional epidemiology: applications, needs and new horizons. *Human Genetics*, 2009, **125**(5-6), pp.507-25.

48. Bates BT, Zhang SN, Dufek JS, et al. The effects of sample size and variability on the correlation coefficient. *Medicine and Science in Sports and Exercise*, 1996, **28**(3), pp.386-391.

49. Bates B, Lennox A, Prentice A, et al. *Appendix P Methods of blood analysis and quality control* [online]. 2014. [Accessed 20 April 2016]. Available from: https://www.food.gov.uk/sites/default/files/media/document/ndns-appendix-p.pdf

50. Macrae R. *HPLC in food analysis.* Food science and technology. 2nd ed. London: Academic, 1988.

51. Vuilleumier JP and Keck E. Fluorometric Assay of Vitamin-C in Biological-Materials Using a Centrifugal Analyzer with Fluorescence Attachment. *Journal of Micronutrient Analysis*, 1989, **5**(1), pp.25-34.

52. Pollard J, Wild CP, White KL, et al. Comparison of plasma biomarkers with dietary assessment methods for fruit and vegetable intake. *European Journal of Clinical Nutrition*, 2003, **57**(8), pp.988-98.

53. Pollard J GD, Kirk S and Cade J. Lifestyle factors affecting fruit and vegetable consumption in the UKWomen's Cohort Study. *Appetite*, 2001, pp.71-79.

54. Pollard J, Greenwood D, Kirk S, et al. Motivations for fruit and vegetable consumption in the UK Women's Cohort Study. *Public Health Nutrition*, 2002, **5**(3), pp.479-86.

55. Pollard J, Kirk SF and Cade JE. Factors affecting food choice in relation to fruit and vegetable intake: a review. *Nutrition Research Reviews*, 2002, **15**(2), pp.373-87.

56. Costa PT, Mccrae RR and Kay GG. Persons, Places, and Personality - Career Assessment Using the Revised Neo Personality-Inventory. *Journal of Career Assessment*, 1995, **3**(2), pp.123-139.

57. Hintsanen M, Puttonen S, Smith K, et al. Five-Factor Personality Traits and Sleep: Evidence From Two Population-Based Cohort Studies. *Health Psychology*, 2014, **33**(10), pp.1214-1223.

58. Kim HN, Cho J, Chang Y, et al. Association between Personality Traits and Sleep Quality in Young Korean Women. *PloS One*, 2015, **10**(6).

59. Duggan KA, Friedman HS, Mcdevitt EA, et al. Personality and Healthy Sleep: The Importance of Conscientiousness and Neuroticism. *PloS One*, 2014, **9**(3).

60. Touchette E, Petit D, Paquet J, et al. Factors associated with fragmented sleep at night across early childhood. *Archives of Pediatrics and Adolescent Medicine*, 2005, **159**(3), pp.242-249.

61. Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*, 2015, **1**(1), pp.40-43.

62. Webb WB and Agnew HWJ. Sleep Stage Characterisfics of Long and Short Sleepers. *Science*, 1970, **168**(3927), pp.146-7.

63. Webb W and Friel J. Sleep Stage and Personality Characteristics of "Natural" Long and Short Sleepers. *Science*, 1971, **171**(3971), pp.587-8.

64. Patel SR, Blackwell T, Ancoli-Israel S, et al. Sleep characteristics of self-reported long sleepers. *Sleep*, 2012, **35**(5), pp.641-8.

65. Youngstedt SD and Kripke DF. Long sleep and mortality: rationale for sleep restriction. *Sleep Medicine Reviews*, 2004, **8**(3), pp.159-74.

66. Patel SR, Malhotra A, Gottlieb DJ, et al. Correlates of Long Sleep Duration. *Sleep*, 2006, **29**(7), pp.881-9.

67. Rayward AT, Duncan MJ, Brown WJ, et al. A cross-sectional cluster analysis of the combined association of physical activity and sleep with sociodemographic and health characteristics in mid-aged and older adults. *Maturitas*, 2017, **102**, pp.56-61.

68. Wakasugi M, Kazama JJ, Narita I, et al. Association between combined lifestyle factors and non-restorative sleep in Japan: a cross-sectional study based on a Japanese health database. *PloS One*, 2014, **9**(9), p.e108718.

69. Wang S, Li B, Wu Y, et al. Relationship of Sleep Duration with Sociodemographic Characteristics, Lifestyle, Mental Health, and Chronic Diseases in a Large Chinese Adult Population. *Journal of Clinical Sleep Medicine*, 2017, **13**(3), pp.377-384.

70. Sekine M, Tatsuse T, Cable N, et al. U-shaped associations between time in bed and the physical and mental functioning of Japanese civil servants: the roles of work, family, behavioral and sleep quality characteristics. *Sleep Medicine*, 2014, **15**(9), pp.1122-31.

71. Zhan Y, Chen R and Yu J. Sleep duration and abnormal serum lipids: the China Health and Nutrition Survey. *Sleep Medicine*, 2014, **15**(7), pp.833-9.

72. Tan NYQ, Chew M, Tham YC, et al. Associations between sleep duration, sleep quality and diabetic retinopathy. *PloS One*, 2018, **13**(5), p.e0196399.

73. Wu L and Sun DL. Sleep duration and falls: a systemic review and meta-analysis of observational studies. *Journal of Sleep Research*, 2017, **26**(3), pp.293-301.

74. Grandner MA, Jackson NJ, Izci-Balserak B, et al. Social and Behavioral Determinants of Perceived Insufficient Sleep. *Frontiers in Neurology*, 2015, **6**, p.112.

75. Whinnery J, Jackson N, Rattanaumpawan P, et al. Short and long sleep duration associated with race/ethnicity, sociodemographics, and socioeconomic position. *Sleep*, 2014, **37**(3), pp.601-11.

76. Ohida T, Kamal AM, Uchiyama M, et al. The influence of lifestyle and health status factors on sleep loss among the japanese general population. *Sleep*, 2001, **24**(3), pp.333-8.

77. Stamatakis KA, Kaplan GA and Roberts RE. Short sleep duration across income, education and race/ethnic groups: Population prevalence and growing disparities over 34 years of follow-up. *Annals of Epidemiology*, 2007, **17**(12), pp.948-55.

78. Vezina-Im LA, Lebel A, Gagnon P, et al. Individual Correlates of Sleep Among Childbearing Age Women in Canada. *Behavioral Sleep Medicine*, 2018, pp.1-12.

79. Vezina-Im LA, Moreno JP, Thompson D, et al. Individual, social and environmental determinants of sleep among women: protocol for a systematic review and meta-analysis. *BMJ Open*, 2017, **7**(6), p.e016592.

80. Johnson BT and Acabchuk RL. What are the keys to a longer, happier life? Answers from five decades of health psychology research. *Social Science and Medicine*, 2018, **196**, pp.218-226.

81. Perry GS, Patil SP and Presley-Cantrell LR. Raising Awareness of Sleep as a Healthy Behavior. *Preventing Chronic Disease*, 2013, **10**.

82. Heffron TM. *Sleep Well, Be Well: A national health priority* [online]. 2014. [Accessed 15 January 2019]. Available from: http://sleepeducation.org/news/2014/05/16/sleep-well-be-well-a-national-health-priority

83. Kakinuma M, Takahashi M, Kato N, et al. Effect of brief sleep hygiene education for workers of an information technology company. *Industrial Health*, 2010, **48**(6), pp.758-65.

84. Chen PH, Kuo HY and Chueh KH. Sleep Hygiene Education: Efficacy on Sleep Quality in Working Women. *Journal of Nursing Research*, 2010, **18**(4), pp.283-289.

85. Galland BC and Mitchell EA. Helping children sleep. *Archives of Disease in Childhood*, 2010, **95**(10), pp.850-853.

86. Tan E, Healey D, Gray AR, et al. Sleep hygiene intervention for youth aged 10 to 18 years with problematic sleep: a before-after pilot study. *BMC Pediatrics*, 2012, **12**, p.189.

87. Golem DL, Martin-Biggers JT, Koenings MM, et al. An integrative review of sleep for nutrition professionals. *Advances in Nutrition*, 2014, **5**(6), pp.742-59.

88. NHS. *The Eatwell Guide* [online]. 2019. [Accessed 15 March 2019]. Available from: https://www.nhs.uk/live-well/eat-well/the-eatwell-guide/

89. Rekhy R and Mcconchie R. Promoting consumption of fruit and vegetables for better health. Have campaigns delivered on the goals? *Appetite*, 2014, **79**, pp.113-123.

90. Dashti HS, Follis JL, Smith CE, et al. Habitual sleep duration is associated with BMI and macronutrient intake and may be modified by CLOCK genetic variants. *The American Journal of Clinical Nutrition*, 2015, **101**(1), pp.135-43.

91. Coborn JE, Houser MM, Perez-Leighton CE, et al. Role of sex and the environment in moderating weight gain due to inadequate sleep. *Current Obesity Reports*, 2017, **6**(4), pp.397-404.

92. Carrier J, Semba K, Deurveilher S, et al. Sex differences in age-related changes in the sleep-wake cycle. *Frontiers in Neuroendocrinology*, 2017, **47**, pp.66-85.

93. Lord C, Sekerovic Z and Carrier J. Sleep regulation and sex hormones exposure in men and women across adulthood. *Pathologie Biologie*, 2014, **62**(5), pp.302-10.

94. Siontis GCM and Ioannidis JPA. Risk factors and interventions with statistically significant tiny effects. *International Journal of Epidemiology*, 2011, **40**(5), pp.1292-1307.

95. Allison DB, Brown AW, George BJ, et al. Reproducibility: A tragedy of errors. *Nature*, 2016, **530**(7588), pp.27-9.

96. Borland SE, Robinson SM, Crozier SR, et al. Stability of dietary patterns in young women over a 2-year period. *European Journal of Clinical Nutrition*, 2008, **62**(1), pp.119-26.

97. Jankovic N, Steppel MT, Kampman E, et al. Stability of dietary patterns assessed with reduced rank regression; the Zutphen Elderly Study. *Nutrition Journal*, 2014, **13**, p.30.

98. Crozier SR, Robinson SM, Godfrey KM, et al. Women's Dietary Patterns Change Little from Before to During Pregnancy. *Journal of Nutrition*, 2009, **139**(10), pp.1956-1963.

99. Newby PK, Weismayer C, Akesson A, et al. Long-term stability of food patterns identified by use of factor analysis among Swedish women. *Journal of Nutrition*, 2006, **136**(3), pp.626-633.

100. Fitt E, Mak TN, Stephen AM, et al. Disaggregating composite food codes in the UK National Diet and Nutrition Survey food composition databank. *European Journal of Clinical Nutrition*, 2010, **64 Suppl 3**, pp.S32-6.

101. Kitamura S, Katayose Y, Nakazaki K, et al. Estimating individual optimal sleep duration and potential sleep debt. *Scientific Reports*, 2016, **6**, p.35812.

102. Goel N, Banks S, Mignot E, et al. DQB1*0602 predicts interindividual differences in physiologic sleep, sleepiness, and fatigue. *Neurology*, 2010, **75**(17), pp.1509-19.

103. Goel N and Dinges DF. Behavioral and genetic markers of sleepiness. *Journal of Clinical Sleep Medicine*, 2011, **7**(5 Suppl), pp.S19-21.

104. Goel N. “Omics” approaches for sleep and circadian rhythm research: Biomarkers for identifying differential vulnerability to sleep loss. *Current Sleep Medicine Reports*, 2015, **1**(1), pp.38-46.

105. Goel N. Genetic Markers of Sleep and Sleepiness. *Sleep Medicine Clinics*, 2017, **12**(3), pp.289-299.

106. Basner M, Fomberstein KM, Razavi FM, et al. American time use survey: Sleep time and its relationship to waking activities. *Sleep*, 2007, **30**(9), pp.1085-95.

107. Basner M, Spaeth AM and Dinges DF. Sociodemographic characteristics and waking activities and their role in the timing and duration of sleep. *Sleep*, 2014, **37**(12), pp.1889-906.

108. Dautovich ND, Shoji KD and Mccrae CS. Variety is the Spice of Life: A Microlongitudinal Study Examining Age Differences in Intraindividual Variability in Daily Activities in Relation to Sleep Outcomes. *Journals of Gerontology. Series B: Psychological Sciences and Social Sciences*, 2015, **70**(4), pp.581-90.

109. Olds TS, Maher CA and Matricciani L. Sleep duration or bedtime? Exploring the relationship between sleep habits and weight status and activity patterns. *Sleep*, 2011, **34**(10), pp.1299-307.

110. Pot GK. Sleep and dietary habits in the urban environment: the role of chrono-nutrition. *Proceedings of the Nutrition Society*, 2018, **77**(3), pp.189-198.

111. Campanini MZ, Guallar-Castillon P, Rodriguez-Artalejo F, et al. Mediterranean Diet and Changes in Sleep Duration and Indicators of Sleep Quality in Older Adults. *Sleep*, 2017, **40**(3).

112. Grandner MA, Jackson N, Gerstner JR, et al. Sleep symptoms associated with intake of specific dietary nutrients. *Journal of Sleep Research*, 2014, **23**(1), pp.22-34.

113. Slavin JL and Lloyd B. Health benefits of fruits and vegetables. *Advances in Nutrition*, 2012, **3**(4), pp.506-16.

114. St-Onge MP, Roberts A, Shechter A, et al. Fiber and Saturated Fat Are Associated with Sleep Arousals and Slow Wave Sleep. *Journal of Clinical Sleep Medicine*, 2016, **12**(1), pp.19-24.

115. Spaeth AM, Dinges DF and Goel N. Objective Measurements of Energy Balance Are Associated With Sleep Architecture in Healthy Adults. *Sleep*, 2017, **40**(1).

116. Manach C, Scalbert A, Morand C, et al. Polyphenols: food sources and bioavailability. *The American Journal of Clinical Nutrition*, 2004, **79**(5), pp.727-47.

117. Scalbert A, Johnson IT and Saltmarsh M. Polyphenols: antioxidants and beyond. *American Journal of Clinical Nutrition*, 2005, **81**(1), pp.215s-217s.

118. Christou K, Moulas AN, Pastaka C, et al. Antioxidant capacity in obstructive sleep apnea patients. *Sleep Medicine*, 2003, **4**(3), pp.225-8.

119. Baldwin CM, Bell IR, Kroesen KW, et al. Differences in antioxidant intake in veterans with and without obstructive sleep apnea. *Sleep*, 2003, **26**, pp.A212-A213.

120. Ford ES, Mokdad AH, Giles WH, et al. The metabolic syndrome and antioxidant concentrations: findings from the Third National Health and Nutrition Examination Survey. *Diabetes*, 2003, **52**(9), pp.2346-52.

121. Baldwin CM, Bootzin RR, Schwenke DC, et al. Antioxidant nutrient intake and supplements as potential moderators of cognitive decline and cardiovascular disease in obstructive sleep apnea. *Sleep Medicine Reviews*, 2005, **9**(6), pp.459-76.

122. Doo M and Kim Y. The Consumption of Dietary Antioxidant Vitamins Modifies the Risk of Obesity among Korean Men with Short Sleep Duration. *Nutrients*, 2017, **9**(7).

123. Pennington JaT and Fisher RA. Food component profiles for fruit and vegetable subgroups. *Journal of Food Composition and Analysis*, 2010, **23**(5), pp.411-418.

124. Al-Juhaimi F, Ghafoor K, Ozcan MM, et al. Effect of various food processing and handling methods on preservation of natural antioxidants in fruits and vegetables. *Journal of Food Science and Technology*, 2018, **55**(10), pp.3872-3880.

125. Al Khatib HK, Hall WL, Creedon A, et al. Sleep extension is a feasible lifestyle intervention in free-living adults who are habitually short sleepers: a potential strategy for decreasing intake of free sugars? A randomized controlled pilot study. *The American Journal of Clinical Nutrition*, 2018, **107**(1), pp.43-53.

126. Ruiter ME, Decoster J, Jacobs L, et al. Normal sleep in African-Americans and Caucasian-Americans: A meta-analysis. *Sleep Medicine*, 2011, **12**(3), pp.209-14.

127. Ruiter ME, Decoster J, Jacobs L, et al. Sleep Disorders in African Americans and Caucasian Americans: A Meta-Analysis. *Behavioral Sleep Medicine*, 2010, **8**(4), pp.246-259.

128. Petrov ME and Lichstein KL. Differences in sleep between black and white adults: an update and future directions. *Sleep Medicine*, 2016, **18**, pp.74-81.

129. Grandner MA, Williams NJ, Knutson KL, et al. Sleep disparity, race/ethnicity, and socioeconomic position. *Sleep Medicine*, 2016, **18**, pp.7-18.

130. Smith SL, Ludy MJ and Tucker RM. Changes in taste preference and steps taken after sleep curtailment. *Physiology and Behavior*, 2016, **163**, pp.228-233.

131. Simon SL, Field J, Miller LE, et al. Sweet/dessert foods are more appealing to adolescents after sleep restriction. *PloS One*, 2015, **10**(2), p.e0115434.

132. Chennaoui M, Arnal PJ, Sauvet F, et al. Sleep and exercise: a reciprocal issue? *Sleep Medicine Reviews*, 2015, **20**, pp.59-72.

133. Espie CA, Luik AI, Cape J, et al. Digital Cognitive Behavioural Therapy for Insomnia versus sleep hygiene education: the impact of improved sleep on functional health, quality of life and psychological well-being. Study protocol for a randomised controlled trial. *Trials*, 2016, **17**(1), p.257.

134. Geiker NRW, Astrup A, Hjorth MF, et al. Does stress influence sleep patterns, food intake, weight gain, abdominal obesity and weight loss interventions and vice versa? *Obesity Reviews*, 2018, **19**(1), pp.81-97.

135. Pilcher JJ, Morris DM, Donnelly J, et al. Interactions between sleep habits and self-control. *Frontiers in Human Neuroscience*, 2015, **9**.

136. Hagger MS. Where does sleep fit in models of self-control and health behaviour? *Stress Health*, 2014, **30**(5), pp.425-30.

Appendices

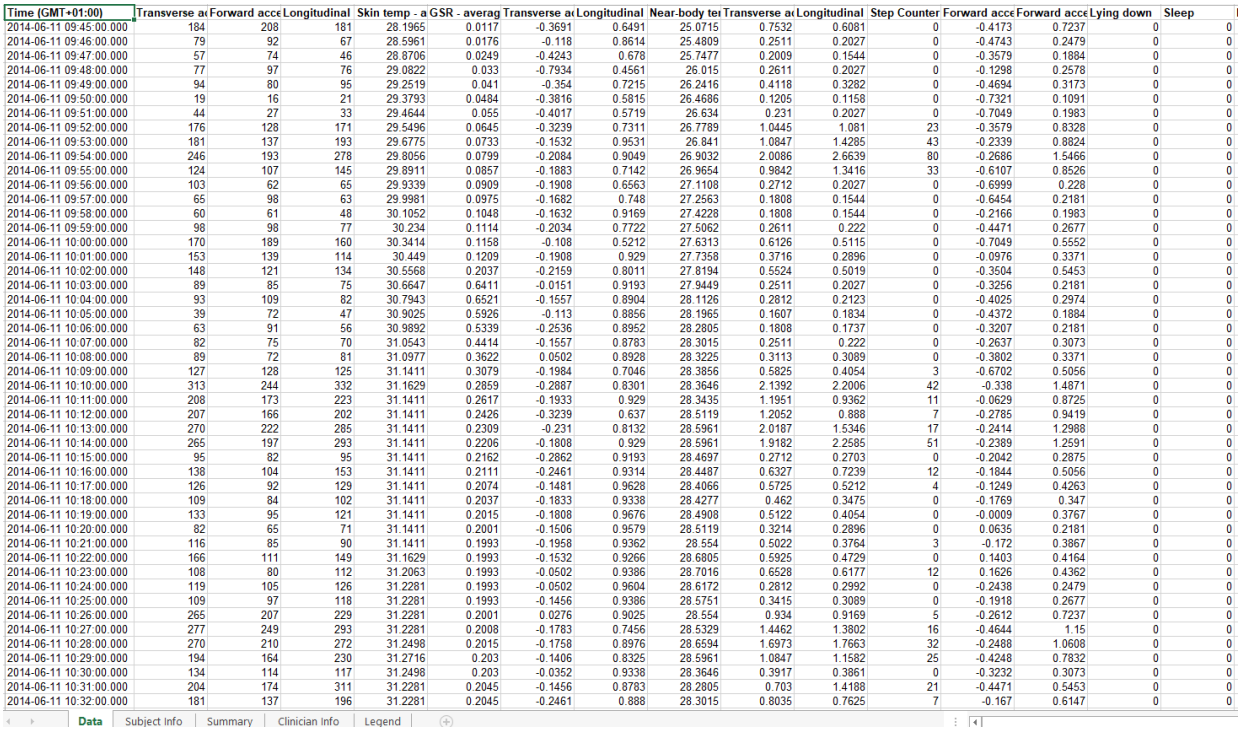
Appendix A: Supplementary information for Chapter 1

Appendix A.1. Search terms used for literature review

1. SLEEP/
2. sleep.tw.
3. or/1-2 [sleep]
4. exp Fruit/
5. exp Citrus/
6. exp VEGETABLES/
7. or/4-6 [fruit or vegetables]
8. (food adj2 intake*).tw.
9. (dietary pattern or dietary habit*).tw.
10. food consumption.tw.
11. Food Habits/
12. Food Preferences/
13. Nutritional status/
14. Nutritional assessment/
15. Diet/
16. Health behavior/
17. diet*.tw.
18. Eating/
19. eating.tw.
20. or/8-19 [diet terms]
21. 7 or 20 [fruit or veg or diet]
22. 3 and 21 [sleep and fruit or veg or diet]
23. (exp adolescent/ or exp child/ or exp newborn/) not ((exp adult/ or exp aged/ or exp middle aged/) and (exp adolescent/ or exp child/ or exp newborn/))
24. 22 not 23 [adult only results]
25. exp animals/ not exp humans/
26. 24 not 25 [human only studies]
27. exp BIOMARKERS/
28. biomarkers.tw.
29. or/27-28 [biomarkers]
30. 3 and 29
31. exp POLYPHENOLS/
32. polyphenols.tw.
33. or/31-32 [polyphenols]
34. 3 and 33

Appendix B: Supplementary information for Chapter 2

Appendix B.1. Sleep variables obtained from actimetric data



Time (GMT+01:00)	Transverse ac	Forward acce	Longitudinal	Skin temp - a	GSR - averag	Transverse ac	Longitudinal	Near-body te	Transverse ac	Longitudinal	Step Counter	Forward acce	Forward acce	Lying down	Sleep
2014-06-11 09:45:00.000	184	208	181	28.1965	0.0117	-0.3691	0.6491	25.0715	0.7532	0.6081	0	-0.4173	0.7237	0	0
2014-06-11 09:46:00.000	79	92	67	28.5961	0.0176	-0.118	0.8614	25.4809	0.2511	0.2027	0	-0.4743	0.2479	0	0
2014-06-11 09:47:00.000	57	74	46	28.8706	0.0249	-0.4243	0.678	25.7477	0.2009	0.1544	0	-0.3579	0.1884	0	0
2014-06-11 09:48:00.000	77	97	76	29.0822	0.033	-0.7934	0.4561	26.015	0.2611	0.2027	0	-0.1298	0.2578	0	0
2014-06-11 09:49:00.000	94	80	95	29.2519	0.041	-0.354	0.7215	26.2416	0.4118	0.3282	0	-0.4694	0.3173	0	0
2014-06-11 09:50:00.000	19	16	21	29.3793	0.0484	-0.3816	0.5815	26.4686	0.1205	0.1158	0	-0.7321	0.1091	0	0
2014-06-11 09:51:00.000	44	27	33	29.4644	0.055	-0.4017	0.5719	26.634	0.231	0.2027	0	-0.7049	0.1983	0	0
2014-06-11 09:52:00.000	176	128	171	29.5496	0.0645	-0.3239	0.7311	26.7789	1.0445	1.081	23	-0.3579	0.8328	0	0
2014-06-11 09:53:00.000	181	137	193	29.6775	0.0733	-0.1532	0.9531	26.841	1.0847	1.4285	43	-0.2339	0.8824	0	0
2014-06-11 09:54:00.000	246	193	278	29.8056	0.0799	-0.2084	0.9049	26.9032	2.0086	2.6639	80	-0.2686	1.5466	0	0
2014-06-11 09:55:00.000	124	107	145	29.8911	0.0857	-0.1883	0.7142	26.9654	0.9842	1.3416	33	-0.6107	0.8526	0	0
2014-06-11 09:56:00.000	103	62	65	29.9339	0.0909	-0.1908	0.6563	27.1108	0.2712	0.2027	0	-0.6999	0.228	0	0
2014-06-11 09:57:00.000	65	98	63	29.9981	0.0975	-0.1682	0.748	27.2563	0.1808	0.1544	0	-0.6454	0.2181	0	0
2014-06-11 09:58:00.000	60	61	48	30.1052	0.1048	-0.1632	0.9169	27.4228	0.1808	0.1544	0	-0.2166	0.1983	0	0
2014-06-11 09:59:00.000	98	98	77	30.234	0.1114	-0.2034	0.7722	27.5062	0.2611	0.222	0	-0.4471	0.2677	0	0
2014-06-11 10:00:00.000	170	189	160	30.3414	0.1158	-0.108	0.5212	27.6313	0.6126	0.5115	0	-0.7049	0.5552	0	0
2014-06-11 10:01:00.000	153	139	114	30.449	0.1209	-0.1908	0.929	27.7358	0.3716	0.2896	0	-0.0976	0.3371	0	0
2014-06-11 10:02:00.000	148	121	134	30.5568	0.2037	-0.2159	0.8011	27.8194	0.5524	0.5019	0	-0.3504	0.5453	0	0
2014-06-11 10:03:00.000	89	85	75	30.6647	0.6411	-0.0151	0.9193	27.9449	0.2511	0.2027	0	-0.3256	0.2181	0	0
2014-06-11 10:04:00.000	93	109	82	30.7943	0.6521	-0.1557	0.8904	28.1126	0.2812	0.2123	0	-0.4025	0.2974	0	0
2014-06-11 10:05:00.000	39	72	47	30.9025	0.5926	-0.113	0.8856	28.1965	0.1607	0.1834	0	-0.4372	0.1884	0	0
2014-06-11 10:06:00.000	63	91	56	30.9892	0.5339	-0.2536	0.8952	28.2805	0.1808	0.1737	0	-0.3207	0.2181	0	0
2014-06-11 10:07:00.000	82	75	70	31.0543	0.4414	-0.1557	0.8783	28.3015	0.2511	0.222	0	-0.2637	0.3073	0	0
2014-06-11 10:08:00.000	89	72	81	31.0977	0.3622	0.0502	0.8928	28.3225	0.3113	0.3089	0	-0.3802	0.3371	0	0
2014-06-11 10:09:00.000	127	128	125	31.1411	0.3079	-0.1984	0.7046	28.3856	0.5825	0.4054	3	-0.6702	0.5056	0	0
2014-06-11 10:10:00.000	313	244	332	31.1629	0.2859	-0.2887	0.8301	28.3646	2.1392	2.2006	42	-0.338	1.4871	0	0
2014-06-11 10:11:00.000	208	173	223	31.1411	0.2617	-0.1933	0.929	28.3435	1.1951	0.9362	11	-0.0629	0.8725	0	0
2014-06-11 10:12:00.000	207	166	202	31.1411	0.2426	-0.3239	0.637	28.5119	1.2052	0.888	7	-0.2785	0.9419	0	0
2014-06-11 10:13:00.000	270	222	285	31.1411	0.2309	-0.231	0.8132	28.5961	2.0187	1.5346	17	-0.2414	1.2988	0	0
2014-06-11 10:14:00.000	265	197	293	31.1411	0.2206	-0.1808	0.929	28.5961	1.9182	2.2585	51	-0.2389	1.2591	0	0
2014-06-11 10:15:00.000	95	82	95	31.1411	0.2162	-0.2862	0.9193	28.4697	0.2712	0.2703	0	-0.2042	0.2875	0	0
2014-06-11 10:16:00.000	138	104	153	31.1411	0.2111	-0.2461	0.9314	28.4487	0.6327	0.7239	12	-0.1844	0.5056	0	0
2014-06-11 10:17:00.000	126	92	129	31.1411	0.2074	-0.1481	0.9628	28.4066	0.5725	0.5212	4	-0.1249	0.4263	0	0
2014-06-11 10:18:00.000	109	84	102	31.1411	0.2037	-0.1833	0.9338	28.4277	0.462	0.3475	0	-0.1769	0.347	0	0
2014-06-11 10:19:00.000	133	95	121	31.1411	0.2015	-0.1808	0.9676	28.4908	0.5122	0.4054	0	-0.0009	0.3767	0	0
2014-06-11 10:20:00.000	82	65	71	31.1411	0.2001	-0.1506	0.9579	28.5119	0.3214	0.2896	0	0.0635	0.2181	0	0
2014-06-11 10:21:00.000	116	85	90	31.1411	0.1993	-0.1958	0.9362	28.554	0.5022	0.3764	3	-0.172	0.3867	0	0
2014-06-11 10:22:00.000	166	111	149	31.1629	0.1993	-0.1532	0.9266	28.6805	0.5925	0.4729	0	0.1403	0.4164	0	0
2014-06-11 10:23:00.000	108	80	112	31.2063	0.1993	-0.0502	0.9386	28.7016	0.6528	0.6177	12	0.1626	0.4362	0	0
2014-06-11 10:24:00.000	119	105	126	31.2281	0.1993	-0.0502	0.9604	28.6172	0.2812	0.2992	0	-0.2438	0.2479	0	0
2014-06-11 10:25:00.000	109	97	118	31.2281	0.1993	-0.1456	0.9386	28.5751	0.3415	0.3089	0	-0.1918	0.2677	0	0
2014-06-11 10:26:00.000	265	207	229	31.2281	0.2001	0.0276	0.9025	28.554	0.934	0.9169	5	-0.2612	0.7237	0	0
2014-06-11 10:27:00.000	277	249	293	31.2281	0.2008	-0.1783	0.7456	28.5329	1.4462	1.3802	16	-0.4644	1.15	0	0
2014-06-11 10:28:00.000	270	210	272	31.2498	0.2015	-0.1758	0.8976	28.6594	1.6973	1.7663	32	-0.2488	1.0608	0	0
2014-06-11 10:29:00.000	194	164	230	31.2716	0.203	-0.1406	0.8325	28.5961	1.0847	1.1582	25	-0.4248	0.7832	0	0
2014-06-11 10:30:00.000	134	114	117	31.2498	0.203	-0.0352	0.9338	28.3646	0.3917	0.3861	0	-0.3232	0.3073	0	0
2014-06-11 10:31:00.000	204	174	311	31.2281	0.2045	-0.1456	0.8783	28.2805	0.703	1.4188	21	-0.4471	0.5453	0	0
2014-06-11 10:32:00.000	181	137	196	31.2281	0.2045	-0.2461	0.888	28.3015	0.8035	0.7625	7	-0.167	0.6147	0	0

Data | Subject Info | Summary | Clinician Info | Legend

This is an example of an excel sheet for a participant containing actimetric data of physical activity and sleep. The first column on the left is the date and time (each row is a minute), the last column is sleep. Sleep Classification Values: 0 (awake), 1 (asleep). Sleep onset was defined as the first minute of registered sleep in a 20-minute period in which there were ≥ 19 minutes of sleep recorded, this was conducted because it has been shown that this improves agreement between actimetric estimates of sleep and polysomnographic measures. Sleep offset was defined as the first minute of registered wakefulness in a 20-minute period in which there were ≥ 19 minutes of wakefulness or activity recorded. Sleep period was calculated as sleep offset minus sleep onset. Mid-sleep time was calculated as the halfway time in sleep period and was used as a proxy of chronotype. Sleep duration was calculated as the sum of sleeping minutes recorded during the sleep period.

Appendix B.2. Fruit/Vegetable groups according to the National Diet and Nutrition Survey categories

Component type	Subcategory
Fruit	Fresh and canned fruit
	Dried fruit
	Fruit juice
Vegetables	Tomatoes
	Tomato puree
	Brassicaceae
	Yellow, red and dark green leafy
	Other vegetables
	Beans and pulses

Fruit/vegetable variables included the following foods

Fruit

Stewed/cooked fruit e.g. apple, rhubarb, plums. Serving
Mixed fruit. Serving
Apple. Whole fruit
Banana. Whole fruit
Berries e.g. raspberries, strawberries, blueberries, blackcurrants. Handful
Cherries. Handful
Grapefruit. Whole fruit or serving
Grapes. Handful
Mango. Serving
Melon. Serving
Orange. Whole fruit
Orange-like small fruits e.g. satsuma, clementine, mandarin. Whole fruit or serving
Peach, nectarine. Whole fruit or serving
Pear. Whole fruit or serving
Pineapple. Serving
Plum. Whole fruit
Other fruit e.g. pomegranate, kiwi, papaya. Whole fruit or serving
Avocado. Medium avocado
Olives. Handful

Fruit juice

Fruit drinks, J20, squash or cordial. Glass/Carton/250ml
Pure orange juice. Glass/Carton/250ml
Pure grapefruit juice. Glass/Carton/250ml
Other pure fruit/vegetable juice. Glass/Carton/250ml
Fruit smoothie. Glass/Bottle/250ml

Dried fruit

Prunes. Handful
Other dried fruit e.g. raisins, apple rings, cranberries (not with breakfast cereal)

Salad

Coleslaw or other salad vegetables in mayonnaise (e.g. waldorf salad). Serving
Mixed side salad. Serving

Tomatoes

Tomatoes, fresh. Medium tomato
Tomatoes, cooked or tinned. Serving

Brassicaceae

Broccoli. Serving
Cabbage, greens, kale. Serving
Watercress. Serving
Turnip or swede. Serving
Cauliflower. Serving

Yellow, red and dark green leafy
Peppers (sweet). Whole pepper
Spinach. Serving
Sweet potatoes. Serving
Carrots (fresh, frozen, raw, cooked). Serving
Butternut squash. Serving
Other vegetables
Other vegetables (e.g. celeriac, asparagus, fennel, aubergine, pumpkin). Serving
Beetroot. Serving
Celery. Stick
Courgette. Serving
Cucumber. 1 inch/2.5cm
Garlic. Clove
Leeks. Serving
Lettuce. Serving
Onion (red, white, pickled, shallots, spring). Serving
Parsnip. Serving
Peas (frozen, fresh, tinned). Serving
Sweetcorn (tinned or frozen, or corn on the cob). Serving
Vegetarian sausage/burger. Each
Vegetable pieces (too small to be counted as individual veg). Serving
Mushrooms. Serving
Mixed vegetables (e.g. frozen mixed veg). Serving
Total fruit
Fresh and canned fruit +Dried fruit
Total vegetables
Beans and pulses + Brassicaceae + Salad + Tomato+ Yellow, red and dark green leafy+ Other vegetables
Total fruit and vegetables
Total fruit + Total vegetables

Appendix B.3. High Performance Liquid Chromatography analysis for Vitamin C

Principle

Metaphosphoric acid is add to precipitate protein and stabilise the ascorbic acid.
After centrifugation, the supernatant is analysed by reversed phased, ion-pair chromatography on a C_{18} column.
DTT is used to reduce oxidised ascorbic acid (dehydroascorbic acid). The plasma sample is incubated at 45ºC with DTT and reanalysed by HPLC to give total ascorbic acid. Levels of dehydroascorbic acid can be inferred by the difference of the total and reduced form of ascorbic acid.

Equipment

Pipettes: variable 100µl and 50µl.
Refrigerated centrifuge
Water bath
LP3 tubes and caps. Acid washed 1ml auto-sampler vials. Phase Separations: cat no 400611.
18.2MΩ water
Column (Phenomenex Luna C_{18}(2) or Hichrom ACE)
Filtration system for mobile phase.
Guard column 20x4.6 packed with C18 corasil (not required for plasma samples)

Chemicals Acid washed glassware (30% nitric acid)

Chemical	Supplier	Cat No	Quantity	Price
Metaphophoric acid	Sigma	79615	100g	42.60
Ascorbic acid	Sigma	A7506	25g	11.80
Ascorbic acid	Sigma	A0278	25g	20.70
Ascorbic acid Eu Std	Sigma	A1300000	100mg	101.00
Uric acid	Sigma	U2625	25g	28.00
DL dithiothreitol	Sigma	D0632	1g	27.90
Sodium hydroxide	Sigma	S5881	500g	23.60
Sulphamic acid	Sigma	383120	100g	21.60
Acetonitrile (HPLC)	Fisher	10010010	2.5L	21.30
Methanol (HPLC)	Fisher	10674922	2.5L	7.20
Sodium acetate trihydrate	Sigma	S8625	250g	12.40
Glacial acetic acid	Sigma	695092	100ml	24.70
Octylamine	Sigma	O5802	5g	18.20

Reagent preparation

2% Metaphosphoric acid (MPA)
Dissolve 2g in 100ml 18.2MΩ water (stable for 1 week at 4ºC).
2% Metaphophoric acid with 0.5% sulphamic acid
Dissolve 2g MPA and 0.5g sulphamic acid in 100ml 18.2MΩ water (stable for 1 week at 4ºC).
0.1M NaOH
Dissolve 0.4g NaOH in 100ml deionised water (store RT).
DTT (7mg/ml for standards)
Dissolve 7mg in 1ml of 18.2MΩ water (stable at 4ºC for 3 days).
DTT (60mg/ml for total AA measurement)
Require 50µl of 60mg/ml solution of DTT. Therefore weigh 3mg per aliquot and dissolve in 50µl 18.2MΩ water per aliquot (stable at 4ºC for 3 days).
Stock solution preparation

Ascorbic acid (200mg/L)
Pipette 0.5ml of 7mg/ml DTT into an acid-washed 100ml volumetric. Add 20mg ascorbic acid and make up to 100 ml with 18.2MΩ H_2O (stable for 1 week at 4ºC).
Uric acid (200mg/L)
Weigh 20mg uric acid. Transfer to 100ml volumetric. Add 5ml of 0.1M NaOH to dissolve. Make up to 100 ml with 18.2MΩ H_2O.
Preparation of working standards
Ascorbic acid (4µg/ml)

To a 5ml screw-cap plastic tube add
2.5ml 2% MPA
100µl stock AA (200mg/L)
2.4ml 18.2MΩ H_2O
(store on ice and prepare daily).

Ascorbic acid (4µg/ml)/Uric acid (24µg/ml)

To a 5ml screw-cap plastic tube add
2.5ml 2% MPA
100µl stock AA (200mg/L)
600µl stock uric acid (200mg/L)
1.8ml 18.2MΩ H_2O
(store on ice and prepare daily).

Collection of plasma samples

As ascorbic acid is unstable above pH 4.0, samples should be stabilised by putting into MPA as soon as possible after collection.
Blood is collected into Li-heparin tubes and the plasma should be separated as soon as possible. AA in plasma from normal patients should be stable for 2 hours, however AA in plasma from acutely ill patients may be very unstable and so MPA should be added as soon as possible. In these cases it is advisable to collect two samples, adding MPA to one and MPA and DTT to the other for more reliable results for total vitamin C.

Preparation of quality control plasma

Li-heparin plasma from normal subjects is pooled to give a volume of 25-30ml.
The plasma is distributed in 0.5ml aliquots into LP4 tubes and 1.0ml 2% MPA is add to each tube.

Preparation of samples for analysis

Remove the samples and QC's from the freezer. Thaw (mix gently but thoroughly) and centrifuge at 3500rpm at 4º for 15 min. remove 0.5ml of supernatant to 1ml autosampler vial for immediate analysis. Keep on ice.

Conversion of DHAA to AA

After removing the first 0.5ml MPA supernatant for immediate analysis, a second 0.5ml aliquot is transferred to an LP3 tube containing 50µl of 60mg/ml DTT. If DTT was added at collection, further DTT does not need to be added.
Mix, cap and incubate in 45ºC water bath for 2 hours. At the end of the incubation, the tubes are left to cool and then stored for at least 16 hours at -40ºC. The samples are then thawed, mixed and centrifuged prior to analysis as above. These samples are much more stable than those without DTT.

HPLC analysis of AA and total vitamin C

Mobile phase

0.2M sodium acetate/acetic acid buffer: acetonitrile (95:5 v/v) containing 1.6ml/L octylamine (approx 10mM).
In 5L conical flask add 6.8g sodium acetate and dissolve in 1L 18.2MΩ H_2O. Add 8ml glacial acetic acid and mix. Measure 950ml in 1L measuring cylinder and add 50ml acetonitrile and mix then add 3.2ml octylamine. Transfer to emptied 5L flask and mix thoroughly by swirling. Filter using an aqueous filter and transfer to storage bottle. Use immediately or store at 4ºC overnight.

Column

Waters C_{18} Nova-Pak cartridge (8x100mm)
Luna C_{18}(2) (Phenomenex)
Ace (Advanced Chromatography Technologies distributed by Hichrom)

Guard column

Waters 20x46mm packed with C_{18} Corasil (Guard column not needed for plasma samples).

HPLC settings

Pump:	Flow rate	2ml/min
Detector:	UV/VIS	270 or 254nm
Autosampler	Injection volume	25µl

Preparing the HPLC to measure samples

The column is usually left recycling in mobile phase.
Make up fresh mobile phase and replace the old with new, switching to waste.

Prerun column at 2ml/min for 2 hours load 6 samples into autosampler, the first being 7mg/ml DTT and the other 5 a combined ascorbic acid/uric acid standard. Inject the samples and check that the ascorbic acid and uric acid peaks are well separated and that the ascorbic acid peaks are satisfactory. Load the freshly centrifuged samples and run.
After the run switch the mobile phase back to recycle and run at 0.2ml/min.

Calculation of results.

The results are calculated by reference to the peak height of the 4µg/ml ascorbic acid standard.

$$Ascorbic\ acid\ in\ MPA\ extract = \frac{y \times 4}{x}\ \mu g/ml$$

Where *x*=peak height of standard and *y*=peak height of unknown sample.
The result is multiplied by 3 to account for the dilution caused by the MPA.

Column washing

If time is available an overnight wash with filtered water running at 0.5ml/min is beneficial. However if time is short a 100ml water wash at 2-3ml/min will suffice, followed by 50ml water:acetonitrile (1:1 v/v) is run through before running fresh mobile phase through the column to waste. Washing can be at a flow rate up to 3ml/min providing that the pressure does not exceed 100 bar (1400psi).

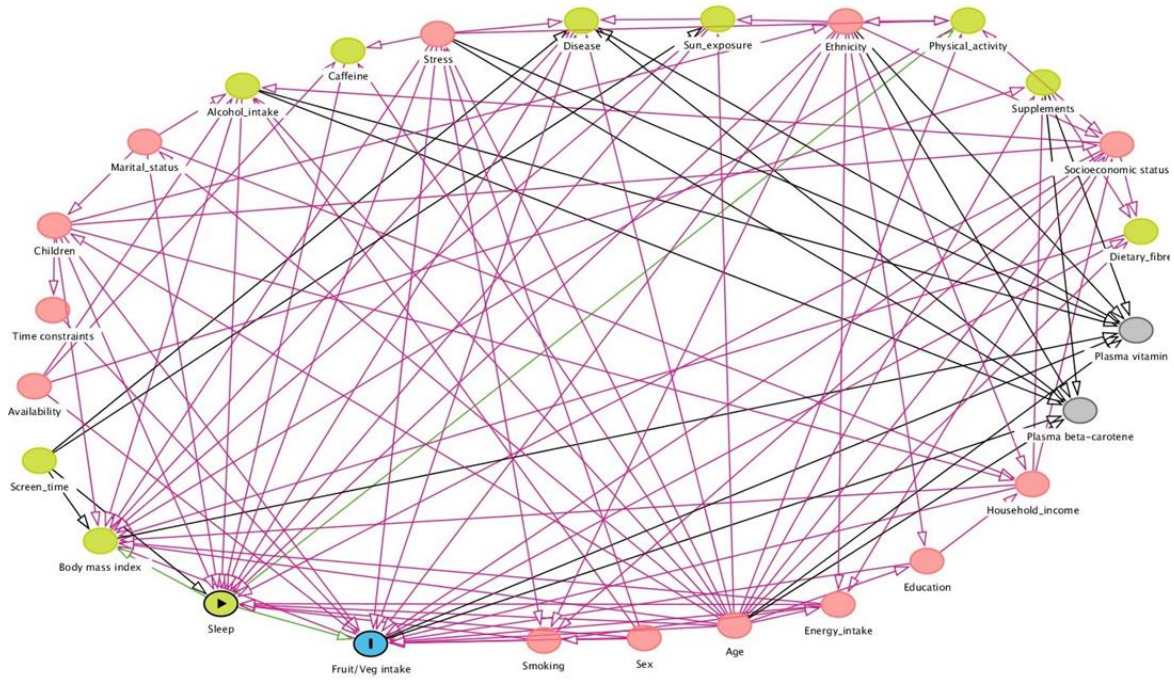
Column storage

After washing the column and rinsing with 50% acetonitrile, the column should be flushed through with 100% acetonitrile and removed for storage.

Common faults

1) The peaks of ascorbic acid and uric acid may not be well separated. This is usually due to a dirty or damaged column. It is possible to add a further 1ml octylamine to the mobile phase followed by refiltering. This will increase the retention time of the two peaks.
2) The ascorbic acid peak may be low. This can be due to the fact that the column is old or needs a wash or that the guard column is void.
3) The ascorbic acid peak height is lower with every injection. Some downward drift may occur during a run but if the drift of the ascorbic acid peak height is more than 4% per hour and is restored by injecting DTT, this is due to oxidising impurities being present in the system. Repacking the guard column or washing the analytical column are the first steps to take. If the problem remains, the stainless steel tubing should be passivated with 30% nitric acid.

Appendix B.4. Directed Acyclic graph



Sleep (exposure)

Fruit and vegetable intake (outcome)

Ancestor of exposure and outcome

Other variables

Appendix C: Supplementary information for Chapter 3

Appendix C.1. Polyphenol classes and sub-classes based on Phenol Explorer.

Flavonoids
Anthocyanins
Chalcones
Dihydrochalcones
Dihydroflavonols
Flavanols
Flavanones
Flavones
Flavonols
Isoflavonoids
Phenolic acids
Hydroxybenzoic acids
Hydroxycinnamic acids
Hydroxyphenylacetic acids
Hydroxyphenylpropanoic acids
Hydroxyphenylpentanoic acids
Stilbenes
Stilbenes
Lignans
Lignans
Other polyphenols
Alkylmethoxyphenols
Alkylphenols
Curcuminoids
Furanocoumarins
Hydroxybenzaldehydes
Hydroxybenzoketones Hydroxycinnamaldehydes
Hydroxycoumarins
Hydroxyphenylpropenes
Methoxyphenols
Naphtoquinones
Phenolic terpenes
Tyrosols
Other polyphenols

Appendix C.2. Sleep duration assessment method in the UK Women's Cohort Study.

ACTIVITY

37. On an average **weekday** how is your day spent?

	Number of hours & / or minutes in a 24 hour day spent doing the following activities?	
	Hours	Minutes
Sleeping		
Sitting		
Light activities (e.g. washing, dressing, eating)		
Standing		
Household chores (e.g. vacuuming, ironing)		
Lifting heavy objects		
Light exercise (e.g. walking, yoga, easy gardening)		
Moderate exercise (e.g. fast walking, easy swimming, hill walking, easy cycling)		
Strenuous exercise (e.g. running, vigorous swimming, high impact aerobics)		

38. On an average **weekend day** how is your day spent?

	Number of hours & / or minutes in a 24 hour day spent doing the following activities?	
	Hours	Minutes
Sleeping		
Sitting		
Light activities (e.g. washing, dressing, eating)		
Standing		
Household chores (e.g. vacuuming, ironing)		
Lifting heavy objects		
Light exercise (e.g. walking, yoga, easy gardening)		
Moderate exercise (e.g. fast walking, easy swimming, hill walking, easy cycling)		
Strenuous exercise (e.g. running, vigorous swimming, high impact aerobics)		

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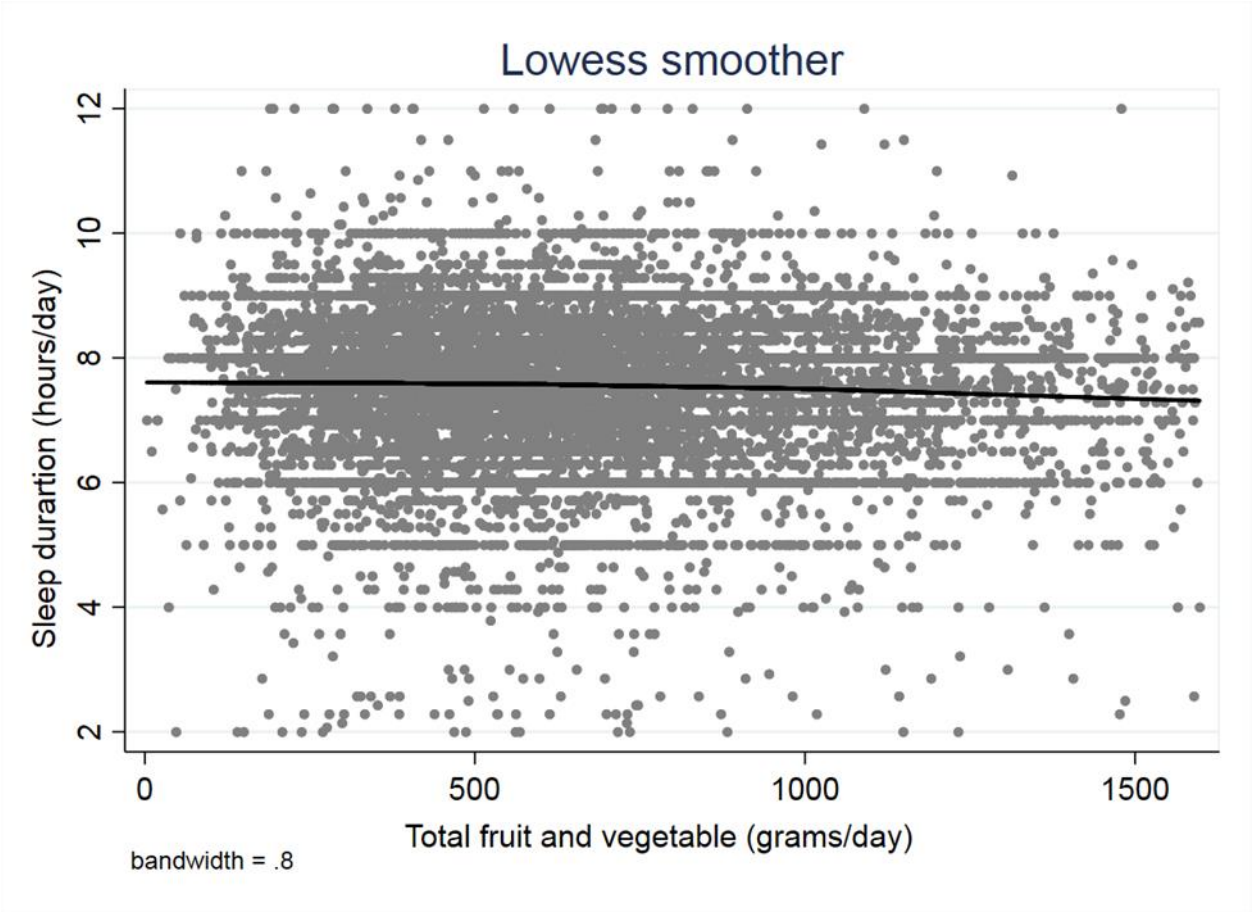
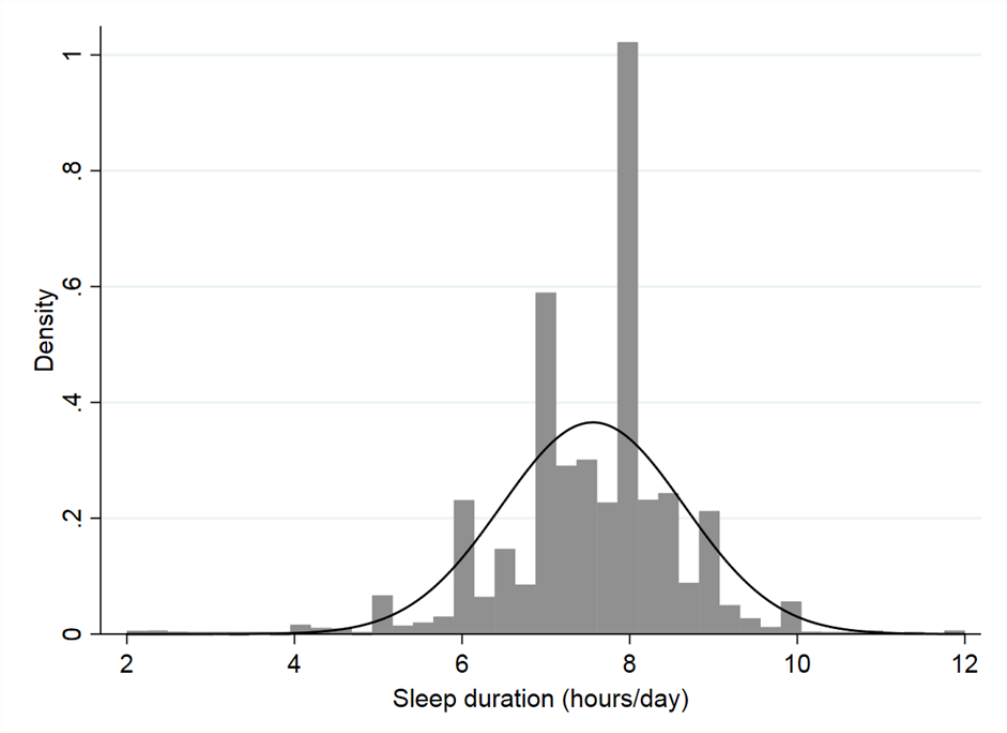
Appendix C.3. The relationship between fruit and vegetable intakes and sleep duration using locally weighted scatterplot smoothing (LOWESS).



Appendix C.4. Normal distribution of sleep duration (outcome) using histogram plot.



Appendix C.5. Prospective associations between polyphenol content from fruit and vegetable intakes and sleep duration for women from the UKWCS stratified by BMI.

Sleep duration (minutes/day)						
	Body mass index <25 kg/m^2 (n=9,017)			Body mass index ≥25 kg/m^2 (n=4,908)		
Polyphenol class	**Coefficient per additional gram (99% CI)***	**P value**	**n**	**Coefficient per additional gram (99% CI)***	**P value**	**n**
Total flavonoids	-32 (-70,4)	0.02	8,336	-23 (-82,35)	0.2	4,480
Total phenolic acids	30 (-430,92)	0.1	8,336	6 (-91, 104)	0.8	4,480
Total other polyphenols	-88 (-264,86)	0.1	8,336	-294 (-681,93)	0.05	4,480
Total stilbenes	-1619 (-8596,5357)	0.5	8,336	1435 (-9291,12162)	0.7	4,480
Total lignans	-21 (-56,13)	0.1	8,336	0.3 (-54,55)	0.9	4,480
Total polyphenols **	-20 (-36,-4)	0.001	8,433	-12 (-38,12)	0.1	4,538

*Adjusted for age, socio-economic status, smoking, ethnicity, total energy intake and other polyphenol components.

**Total polyphenols= the sum of total flavonoids, total phenolic acids, total other polyphenols, total stilbenes and total lignans.

122 pregnant women were excluded

Extreme values of body mass index (<18 and >50 kg/m2) were excluded (n=183)

Appendix C.6. Prospective associations between polyphenol content from fruit and vegetable intakes and sleep duration for women from the UKWCS stratified by vegan/vegetarian status.

	Sleep duration (minutes/day)					
	Vegan or vegetarian (n=4,469)			Non-vegan or non-vegetarian (n=9,455)		
Polyphenol class	**Coefficient per additional gram (99% CI)***	**P value**	**n**	**Coefficient per additional gram (99% CI)***	**P value**	**n**
Total flavonoids	9 (-43,62)	0.6	4,148	-52 (-92,-13)	0.001	8,668
Total phenolic acids	-6 (-96,84)	0.8	4,148	34 (-30,99)	0.1	8,668
Total other polyphenols	-94 (-315,125)	0.2	4,148	-138 (-389,112)	0.1	8,668
Total stilbenes	-4589 (-14484,5305)	0.2	4,148	2380(-4955,9717)	0.4	8,668
Total lignans	-22 (-69,24)	0.2	4,148	-4 (-43,33)	0.7	8,668
Total polyphenols **	-14 (-35,7)	0.08	4,200	-18 (-35,-1)	0.006	8,771

*Adjusted for age, socio-economic status, smoking, ethnicity, total energy intake and other polyphenol components.

**Total polyphenols= the sum of total flavonoids, total phenolic acids, total other polyphenols, total stilbenes and total lignans.

122 pregnant women were excluded

Appendix C.7. Prospective associations between polyphenol content from fruit and vegetable intakes and sleep duration for women from the UKWCS based on weekdays and weekends.

	Sleep duration (minutes/day)					
	Weekdays			Weekends		
Polyphenol class	**Coefficient per additional gram (99% CI)***	**P value**	**n**	**Coefficient per additional gram (99% CI)***	**P value**	**n**
Total flavonoids	-28 (-58,1)	0.02	12,769	-23 (-56,9)	0.07	12,605
Total phenolic acids	43 (-6,93)	0.02	12,769	-4 (-59,50)	0.8	12,605
Total other polyphenols	-90 (-247,66)	0.1	12,769	-61 (-230,107)	0.3	12,605
Total stilbenes	-581 (-6164,5001)	0.7	12,769	-3688 (-9789,2412)	0.1	12,605
Total lignans	-19 (-47,8)	0.07	12,769	-23 (-54,6)	0.04	12,605
Total polyphenols **	-14 (-27,-1)	0.004	12,922	-25 (-39,-11)	<0.001	12,755

*Adjusted for age, socio-economic status, smoking, ethnicity, total energy intake and other polyphenol components.

**Total polyphenols= the sum of total flavonoids, total phenolic acids, total other polyphenols, total stilbenes and total lignans.

122 pregnant women were excluded

Appendix C.8. Prospective associations between polyphenol content from fruit and vegetable intakes and sleep duration for women from the UKWCS based on alcohol consumption frequency.

	Sleep duration (minutes/day)								
	More than once a week			Once a week or less			Never		
Polyphenol class	**Coefficient per additional gram (99% CI)***	**P value**	**n**	**Coefficient per additional 80 g/d (99% CI)***	**P value**	**n**	**Coefficient per additional gram (99% CI)***	**P value**	**n**
Total flavonoids	-44 (-89,-0.7)	0.009	6,633	-8 (-59,42)	0.6	4,662	-27 (-133,78)	0.5	1,271
Total phenolic acids	23 (-49,96)	0.4	6,633	43 (-44,132)	0.2	4,662	- 110 (-274,53)	0.08	1,271
Total other polyphenols	-152 (-357,53)	0.05	6,633	-287 (-648,73)	0.04	4,662	140 (-302,582)	0.4	1,271
Total stilbenes	5000 (-3428,13428)	0.1	6,633	-7235 (-16632,2161)	0.04	4,662	4286 (-13504,22076)	0.5	1,271
Total lignans	4 (-40,49)	0.7	6,633	-33 (-79,13)	0.06	4,662	-26 (-111,59)	0.4	1,271
Total polyphenols **	-11 (-31,8)	0.1	6,677	-23 (-45,-2)	0.005	4,712	-29 (-67,9)	0.05	1,327

*Adjusted for age, socio-economic status, smoking, ethnicity, total energy intake and other polyphenol components.

**Total polyphenols= the sum of total flavonoids, total phenolic acids, total other polyphenols, total stilbenes and total lignans.

122 pregnant women were excluded

Appendix C.9. Prospective associations between polyphenol content from fruit and vegetable intakes and sleep duration for women from the UKWCS after excluding participants who self-reported supplement intake, long-term illness and medication use.

	Sleep duration (minutes/day)								
	Excluding supplement users (n=7,634)			Excluding those with long-term illness (n=3,673)			Excluding those who reported medication use (n=4,165)		
Polyphenol class	**Coefficient per additional gram (99% CI)***	**P value**	**n**	**Coefficient per additional gram (99% CI)***	**P value**	**n**	**Coefficient per additional gram (99% CI)***	**P value**	**n**
Total flavonoids	-36 (-83,11)	0.05	5,786	-27 (-62,8)	0.05	9,584	- 18 (-54,17)	0.1	8,969
Total phenolic acids	56 (-23,136)	0.07	5,786	41 (-20,103)	0.08	9,473	37 (-23,97)	0.1	8,969
Total other polyphenols	- 214 (-449,20)	0.02	5,786	-141 (-324,42)	0.04	9,473	-239 (-421,-56)	0.001	8,969
Total stilbenes	662 (-7887,9211)	0.8	5,786	-3358 (-9941,3223)	0.1	9,473	-1080 (-7762,5600)	0.6	8,969
Total lignans	-14 (-59,31)	0.4	5,786	-18 (-52,14)	0.1	9,473	-9 (-43,25)	0.4	8,969
Total polyphenols **	-15 (-36,4)	0.04	5,845	-18 (-34,-3)	0.001	9,593	-11 (-27,3)	0.04	9,058

*Adjusted for age, socio-economic status, smoking, ethnicity, total energy intake and other polyphenol components.
**Total polyphenols= the sum of total flavonoids, total phenolic acids, total other polyphenols, total stilbenes and total lignans.
122 pregnant women were excluded

Illness that were excluded in Appendix B.9.

Heart attack, coronary thrombosis, myocardial infarction
Angina
Stroke
High bold pressure (Hypertension)
High blood cholesterol (hyperlipidaemia)
Diabetes
Gallstones
Polyps in the large intestine
Cancer

Appendix C.10. Prospective associations between polyphenol content from fruit and vegetable intakes and sleep duration for women from the UKWCS after further adjusting for BMI and physical.

Sleep duration (minutes/day)			
Adjusted* (including BMI and physical activity)			
Polyphenol class	**Coefficient per additional gram (99% CI)**	**P value**	**n**
Total flavonoids	-22 (-60,15)	0.1	7,360
Total phenolic acids	27 (-40,94)	0.2	7,360
Total other polyphenols	-40 (-248,166)	0.6	7,360
Total stilbenes	-1053 (-8105,5999)	0.7	7,360
Total lignans	-13 (-47,21)	0.3	7,360
Total polyphenols **	-11 (-27,4)	0.06	7,424

Legend: BMI (body mass index)

*Adjusted for age, socio-economic status, smoking, ethnicity, total energy intake and other polyphenol components.

**Total polyphenols= the sum of total flavonoids, total phenolic acids, total other polyphenols, total stilbenes and total lignans.

122 pregnant women were excluded

Appendix D: Supplementary information for Chapter 4

Appendix D.1. The association between sleep duration categories and FV intakes and associated biomarkers for adults from the NDNS years 1-4 after excluding participants who consume prescribed medicines.

Sleep categories compared to the reference group (7-8 hours/day)					
Model 2 (n=1044)		**Short sleepers <7 hours/day**		**Long sleepers >8 hours/day**	
FV intake		**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**
Total fruit[a] (g/day)		-13 (-27, -0.4)	0.04	-17 (-34, -0.1)	0.04
Total veg[b] (g/day)		-10 (-24, 4)	0.1	-5 (-24, 2)	0.5
FV portions[c]		-0.2 (-0.5, -.005)	0.04	-0.1 (-0.5, 0.1)	0.3
5-a-day portions[d]		-0.2 (-0.5, -0.0003)	0.05	-0.1 (-0.5, 0.1)	0.3
Total FV [e](g/day)		-24 (-45,-2)	0.03	-23 (-51,4)	0.1
Nutrients (mg)					
Vitamin C diet only		-5 (-13, 2)	0.1	-4(-15,5)	0.3
Vitamin C *		-7 (-24, 10)	0.4	-11 (-33, 11)	0.3
Biomarkers (µmol/l)					
Vitamin C	n= 375	-0.6 (-5, 3)	0.7	5 (-0.09, 11)	0.05
Total caro[f]	n= 294	-0.2 (-0.5, -0.02)	0.03	-0.08 (-0.4, 0.2)	0.5
α-carotene	n= 378	-0.005 (-0.02,0.01)	0.5	-0.009 (-0.03, 0.01)	0.4
β-carotene	n= 402	-0.05 (-0.1, 0.02)	0.1	-0.02(-0.1, 0.07)	0.6
Lycopene	n= 403	-0.06 (-0.1, 0.01)	0.1	-0.06 (-0.1, 0.04)	0.2

Legend: FV (fruits and vegetables), g (gram), l (litre), µmol (micromole), m (milligram), n (number), veg (vegetables).

566 participants reported taking prescribed medicines and were excluded from the analyses.

Model 2 adjusted for age, sex, socio-economic status, smoking, ethnicity and food energy.

[a] Total fruit (not including juice) = Fruit (g) +Dried fruit (g) + Smoothie fruit (g)
[b] Total vegetables= Beans (g) + Brassicaceae (g) + Other Vegg + Tomatoes (g) + Tomato Puree (g) +Yellow Red Green (g).
[c] FV portions= (Fruit (g) + Driedfruitx3_mean + Tompureex5 mean + beans max mean+ Brassicaceae (g) + Yellow Red Green (g) + Other veg (g) + Tomatoes (g)) / 80 .
[d] 5-a-day portions (portions/day) = Fruit veg portions + Fruit juice portions+ Smoothie Fruit portions
[e] Total FV (not including juice) = Total fruit +Total vegetables
[f] Total carotenoids = Lutein + alpha-cryptoxanthin + beta-cryptoxanthin+ lycopene + alpha-carotene + beta-carotene
*Vitamin C including supplements

Appendix D.2. The association between sleep duration categories and FV intakes and associated biomarkers for adults from the NDNS years 1-4 after excluding participants who reported consuming vitamins, minerals and/or supplements in the past year.

Sleep categories compared to the reference group (7-8hours/day)					
Model 2 (n=1084)		**Short sleepers <7 hours/day**		**Long sleepers >8 hours/day**	
FV intake		**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**
Total fruit[a] (g/day)		-5 (-17,7)	0.4	-10 (-25, 0.5)	0.2
Total veg[b] (g/day)		-11 (-24, 1)	0.09	-7 (-24, 8)	0.3
FV portions[c]		-0.1 (-0.4, 0.07)	0.1	-0.1 (-0.4, 0.1)	0.3
5-a-day portions[d]		-0.1 (-0.4, 0.09)	0.2	-0.1 (-0.4, 0.2)	0.4
Total FV[e](g/day)		-16 (-36, 3)	0.1	-17 (-43,7)	0.1
Nutrients (mg)					
Vitamin C diet only		1 (-6, 8)	0.7	2 (-6, 11)	0.5
Vitamin C *		0.2 (-8, 8)	0.9	2 (-7, 13)	0.5
Biomarkers (µmol/l)					
Vitamin C	n= 462	-3 (-7, 0.6)	0.09	6 (1, 11)	0.009
Total caro [f]	n= 330	-0.2 (-0.4, -0.01)	0.03	0.06 (-0.2 ,0.3)	0.6
α-carotene	n= 461	-0.005 (-0.02,0.009)	0.4	0.0007 (-0.01, 0.02)	0.9
β-carotene	n= 492	-0.05 (-0.1, 0.002)	0.06	0.06 (-0.01,0.1)	0.1
Lycopene	n= 490	-0.08 (-0.1, -0.005)	0.03	-0.04 (-0.1, 0.04)	0.3

Legend: FV (fruits and vegetables), g (gram), l (litre), µmol (micromole), m (milligram), n (number), veg (vegetables).

526 participants reported taking vitamins, minerals or supplements in the past year and were excluded from the analyses.

Model 2 adjusted for age, sex, socio-economic status, smoking, ethnicity and food energy.

[a] Total fruit (not including juice) = Fruit (g) +Dried fruit (g) + Smoothie fruit (g)
[b] Total vegetables= Beans (g) + Brassicaceae (g) + Other Vegg + Tomatoes (g) + Tomato Puree (g) +Yellow Red Green (g).
[c] FV portions= (Fruit (g) + Driedfruitx3_mean + Tompureex5 mean + beans max mean+ Brassicaceae (g) + Yellow Red Green (g) + Other veg (g) + Tomatoes (g)) / 80 .
[d] 5-a-day portions (portions/day) = Fruit veg portions + Fruit juice portions+ Smoothie Fruit portions
[e] Total FV (not including juice) = Total fruit +Total vegetables
[f] Total carotenoids = Lutein + alpha-cryptoxanthin + beta-cryptoxanthin+ lycopene + alpha-carotene + beta-carotene
*Vitamin C including supplements

Appendix D.3. The association between sleep duration categories and FV intakes and associated biomarkers for adults from the NDNS years 1-4 after excluding those who have a longstanding illness.

Sleep categories compared to the reference group (7-8hours)					
Model 2 (n= 1063)		**Short sleepers <7 hours**		**Long sleepers >8 hours**	
FV intake		**Mean difference(95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**
Total fruit[a] (g/day)		-15 (-29, -2)	0.02	-9 (-26, 7)	0.2
Total veg[b] (g/day)		-14 (-28, -0.04)	0.04	-10 (-28, 8)	0.2
FV portions[c]		-0.4 (-0.7, -0.1)	0.004	-0.1 (-0.5, 0.1)	0.2
5-a-day portions[d]		-0.4 (-0.7, -0.1)	0.005	-0.1 (-0.5 ,0.1)	0.3
Total FV[e](g/day)		-30 (-52, -8)	0.007	-20 (-48, 8)	0.1
Nutrients (mg)					
Vitamin C diet only		-5 (-14, 2)	0.1	-1 (-11, 9)	0.8
Vitamin C *		-12 (-30, 5)	0.1	-9 (-32, 14)	0.4
Biomarkers (µmol/l)					
Vitamin C	n= 474	-2 (-6, 1)	0.2	4 (-0.4 ,9)	0.07
Total caro[f]	n= 369	-0.3 (-0.5, -0.08)	0.007	-0.04 (-0.3,0.2)	0.7
α-carotene	n= 477	-0.006 (-0.02, 0.01)	0.4	0.001 (-0.01, 0.02)	0.9
β-carotene	n= 506	-0.06 (-0.1, -0.003)	0.03	0.01 (-0.06, 0.09)	0.6
Lycopene	n= 505	-0.07 (-0.1, 0.008)	0.08	-0.05 (-0.1, 0.05)	0.3

Legend: FV (fruits and vegetables), g (gram), l (litre), µmol (micromole), m (milligram), n (number), veg (vegetables).

547 participants reported having a longstanding illness and were excluded from the analyses.

Model 2 adjusted for age, sex, socio-economic status, smoking, ethnicity and food energy.

[a] Total fruit (not including juice) = Fruit (g) +Dried fruit (g) + Smoothie fruit (g)
[b] Total vegetables= Beans (g) + Brassicaceae (g) + Other Vegg + Tomatoes (g) + Tomato Puree (g) +Yellow Red Green (g).
[c] FV portions= (Fruit (g) + Driedfruitx3_mean + Tompureex5 mean + beans max mean+ Brassicaceae (g) + Yellow Red Green (g) + Other veg (g) + Tomatoes (g)) / 80 .
[d] 5-a-day portions (portions/day) = Fruit veg portions + Fruit juice portions+ Smoothie Fruit portions
[e] Total FV (not including juice) = Total fruit +Total vegetables
[f] Total carotenoids = Lutein + alpha-cryptoxanthin + beta-cryptoxanthin+ lycopene + alpha-carotene + beta-carotene
*Vitamin C including supplements

Appendix D.4. The association between sleep duration categories and FV intakes and associated biomarkers for adults from the NDNS years 1-4 after excluding those who reported being vegetarian.

Sleep categories compared to the reference group (7-8hours/day)					
Model 2 (n= 1571)		**Short sleepers <7 hours/day**		**Long sleepers >8 hours/day**	
FV intake		**Mean difference(95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**
Total fruit[a] (g/day)		-14 (-25,-3)	0.009	-9 (-26,7)	0.2
Total veg[b] (g/day)		-11 (-22, 0.1)	0.05	-11 (-25,3)	0.1
FV portions[c]		-0.3 (-0.5, -0.07)	0.009	-0.3 (-0.5, -0.01)	0.03
5-a-day portions[d]		-0.3 (-0.5,-0.08)	0.008	-0.2 (-0.5, 0.008)	0.05
Total FV [e](g/day)		-25 (-43,-8)	0.004	-29 (-51, -7)	0.009
Nutrients (mg)					
Vitamin C diet only		-5 (-12, 0.9)	0.09	-4 (-12, 4)	0.3
Vitamin C *		-4 (-18, 8)	0.4	-8 (-25, 8)	0.3
Biomarkers (µmol/l)					
Vitamin C	n= 702	-3 (-6, 0.1)	0.06	4 (0.09, 8)	0.04
Total caro [f]	n= 506	-0.2 (-0.4, -0.09)	0.003	-0.05 (-0.2, 0.1)	0.6
α-carotene	n= 702	-0.006 (-0.01,0.007)	0.3	-0.002 (-0.01 ,0.01)	0.7
β-carotene	n= 748	-0.05 (-0.1, -0.008)	0.02	0.01 (-0.04, 0.07)	0.6
Lycopene	n= 746	-0.09 (-0.1, -0.03)	0.003	-0.05 (-0.1 0.02)	0.2

Legend: FV (fruits and vegetables), g (gram), l (litre), µmol (micromole), m (milligram), n (number), veg (vegetables).

39 participants reported being vegetarian and were excluded from this analyses.

Model 2 adjusted for age, sex, socio-economic status, smoking, ethnicity and food energy.

[a] Total fruit (not including juice) = Fruit (g) +Dried fruit (g) + Smoothie fruit (g)
[b] Total vegetables= Beans (g) + Brassicaceae (g) + Other Vegg + Tomatoes (g) + Tomato Puree (g) +Yellow Red Green (g).
[c] FV portions= (Fruit (g) + Driedfruitx3_mean + Tompureex5 mean + beans max mean+ Brassicaceae (g) + Yellow Red Green (g) + Other veg (g) + Tomatoes (g)) / 80 .
[d] 5-a-day portions (portions/day) = Fruit veg portions + Fruit juice portions+ Smoothie Fruit portions
[e] Total FV (not including juice) = Total fruit +Total vegetables
[f] Total carotenoids = Lutein + alpha-cryptoxanthin + beta-cryptoxanthin+ lycopene + alpha-carotene + beta-carotene
*Vitamin C including supplements

Appendix D.5. The association between sleep duration categories and FV intakes, nutrients and associated biomarkers for adults from the NDNS years 1-4 after further adjusting for BMI and physical activity.

Sleep categories compared to the reference group (7-8hours/day)					
Model 2 (n=1171)		**Short sleepers <7 hours/day**		**Long sleepers >8 hours/day**	
FV intake		**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**
Total fruit[a] (g/day)		-17(-29,-5)	0.006	-19 (-34, -3)	0.01
Total veg[b] (g/day)		-3 (-16, 9)	0.5	-10 (-26, 6)	0.2
FV portions[c]		-0.2 (-0.5, -0.03)	0.09	-0.3 (-0.6, -0.03)	0.08
5-a-day portions[d]		-0.2 (-0.5, -0.03)	0.08	-0.3 (-0.5 ,0.05)	0.09
Total FV [e](g/day)		-21 (-41, -1)	0.03	-29 (-54, -4)	0.02
Nutrients (mg)					
Vitamin C diet only		-1 (-8, 5)	0.7	-5 (-14, 3)	0.2
Vitamin C *		-9 (-26, 8)	0.3	-12 (-34, 8)	0.2
Biomarkers (µmol/l)					
Vitamin C	n= 550	-2 (-6, 0.7)	0.1	4 (-0.01, 9)	0.05
Total caro [f]	n= 440	-0.2 (-0.4, -0.05)	0.01	-0.04 (-0.2 , 0.2)	0.7
α-carotene	n= 563	-0.002 (-0.01, 0.01)	0.7	-0.002 (-0.02, 0.01)	0.7
β-carotene	n= 588	-0.03 (-0.09 ,0.01)	0.1	0.03 (-0.04, 0.1)	0.4
Lycopene	n= 585	-0.09(-0.1, -0.02)	0.007	-0.01(-0.1, 0.07)	0.7

Legend: BMI (body mass index), FV (fruits and vegetables), g (gram), l (litre), µmol (micromole), m (milligram), n (number), veg (vegetables).

Physical activity was time spent at moderate or vigorous physical activity (hour/day).

Model 2 adjusted for age, sex, socio-economic status, smoking, ethnicity and food energy.

[a] Total fruit (not including juice) = Fruit (g) +Dried fruit (g) + Smoothie fruit (g)
[b] Total vegetables= Beans (g) + Brassicaceae (g) + Other Vegg + Tomatoes (g) + Tomato Puree (g) +Yellow Red Green (g).
[c] FV portions= (Fruit (g) + Driedfruitx3_mean + Tompureex5 mean + beans max mean+ Brassicaceae (g) + Yellow Red Green (g) + Other veg (g) + Tomatoes (g)) / 80 .
[d] 5-a-day portions (portions/day) = Fruit veg portions + Fruit juice portions+ Smoothie Fruit portions
[e] Total FV (not including juice) = Total fruit +Total vegetables
[f] Total carotenoids = Lutein + alpha-cryptoxanthin + beta-cryptoxanthin+ lycopene + alpha-carotene + beta-carotene
*Vitamin C including supplements

Appendix D.6. The association between weekday/weekend sleep duration categories and FV intakes and associated biomarkers for adults from the NDNS year 1-4.

Weekday sleep categories compared to reference group (7-8 hours/day)				
Model 2 (n=1610)	**Short sleepers <7 hours/day**		**Long sleepers >8 hours/day**	
FV intake	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**
Total fruit [a] (g/day)	-13 (-23, -2)	0.01	-28 (-44, -12)	0.001
Total veg [b] (g/day)	-8 (-19, 2)	0.1	-16 (-32, -0.1)	0.04
FV portions[c]	-0.2 (-0.4,-0.02)	0.03	-0.5 (-0.8, -0.1)	0.003
5-a-day portions[d]	-0.2 (-0.4 , -0.03)	0.02	-0.5 (-0.8, -0.1)	0.004
Total FV[e] (g/day)	-21 (-38, -4)	0.01	-44 (-70, -19)	0.001
Nutrients (mg)				
Vitamin C diet only	-3 (-10, 2)	0.2	-8 (-18, 0.9)	0.07
Vitamin C **	-4 (-18, 9)	0.5	-18 (-38, 2)	0.08
Biomarkers(µmol/l)				
Vitamin C n=718	-4 (-7, -0.9)	0.01	0.04 (-4, 4)	0.9
Total caro[f] n= 520	-0.2 (-0.4, -0.06)	0.008	-0.09 (-0.3, 0.1)	0.4
α-carotene n=719	-0.005 (-0.01, 0.007)	0.3	-0.004 (-0.02, 0.01)	0.6
β-carotene n= 765	-0.05 (-0.1, -0.01)	0.01	0.01 (-0.06,0.08)	0.7
Lycopene n= 763	-0.08 (-0.1, -0.01)	0.01	-0.08 (-0.1,0.01)	0.09
Weekend sleep categories compared to reference group (7-8 hours/day)				
Model 2 (n=1610)	**Short sleepers <7 hours/day**		**Long sleepers >8 hours/day**	
FV intake	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**
Total fruit [a] (g/day)	-10 (-22, 1)	0.07	-3 (-15, 8)	0.5
Total veg [b] (g/day)	-14 (-26, -2)	0.01	-6 (-18, 6)	0.3
FV portions[c]	-0.3 (-0.5 ,-0.05)	0.01	-0.1 (-0.3, 0.1)	0.4
5-a-day portions[d]	-0.2 (-0.5,-0.03)	0.02	-0.04 (-0.3, 0.2)	0.7
Total FV[e] (g/day)	-24 (-43, -6)	0.010	-9 (-29, 9)	0.3
Nutrients (mg)				
Vitamin C diet only	-4 (-11, 2)	0.2	4 (-2, 11)	0.2
Vitamin C *	-8 (-23, 6)	0.2	-1 (-17, 13)	0.8
Biomarkers(µmol/l)				
Vitamin C n=717	-4 (-7, -0.6)	0.020	1 (-2, 5)	0.3
Total caro[f] n= 519	-0.2 (-0.4, -0.1)	0.003	-0.05 (-0.2, 0.1)	0.6
α-carotene n= 718	-0.004 (-0.01, 0.009)	0.5	-0.001 (-0.01, 0.01)	0.8
β-carotene n= 764	-0.05(-0.1, -0.0006)	0.04	0.01 (-0.04,0.07)	0.6
Lycopene n= 762	-0.09 (-0.1, -0.03)	0.003	-0.05 (-0.1,0.01)	0.1

Legend: FV (fruits and vegetables), g (gram), l (litre), µmol (micromole), m (milligram), n (number), veg (vegetables).

Model 2 adjusted for age, sex, socio-economic status, smoking, ethnicity and food energy.

[a] Total fruit (not including juice) = Fruit (g) +Dried fruit (g) + Smoothie fruit (g)

[b] Total vegetables= Beans (g) + Brassicaceae (g) + Other Vegg + Tomatoes (g) + Tomato Puree (g) +Yellow Red Green (g).

[c] FV portions= (Fruit (g) + Driedfruitx3_mean + Tompureex5 mean + beans max mean+ Brassicaceae (g) + Yellow Red Green (g) + Other veg (g) + Tomatoes (g)) / 80 .

[d] 5-a-day portions (portions/day) = Fruit veg portions + Fruit juice portions+ Smoothie Fruit portions

[e] Total FV (not including juice) = Total fruit +Total vegetables

[f] Total carotenoids = Lutein + alpha-cryptoxanthin + beta-cryptoxanthin+ lycopene + alpha-carotene + beta-carotene

*Vitamin C including supplements

Appendix D.7. The association between sleep duration categories and FV intakes, nutrients and associated biomarkers for adults from the NDNS years 1-4 stratified by BMI.

Short sleepers (<7h/d) and Long sleepers (>8h/d) compared to the reference group (7-8 h/d) stratified by BMI												
BMI categories	**BMI 18.5-25 n= 524**				**BMI 25-30 n= 525**				**BMI ≥30 n= 438**			
	Short sleepers <7 h/d		**Long sleepers >8 h/d**		**Short sleepers <7 h/d**		**Long sleepers >8 h/d**		**Short sleepers <7 h/d**		**Long sleepers >8 h/d**	
FV intake Model 2	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P Value**
Total fruit[a] (g/day)	-22 (-45,-0.4)	0.04	-26 (-50,-1)	0.03	-8 (-26,9)	0.3	-4 (-27,18)	0.7	-16(-36,2)	0.09	-22 (-51,5)	0.1
Total veg[b] (g/day)	-23 (-45,-1)	0.04	-11 (-35,12)	0.3	3 (-15,23)	0.6	-3 (-27,21)	0.8	-21(-41,-1)	0.03	-24(-53, 3)	0.09
FV portions[c]	-0.6 (-1,0.2)	0.004	-0.4 (-0.8,0.08)	0.1	-0.01 (-0.3,0.3)	0.9	-0.1 (-0.6,0.3)	0.6	-0.3(0.7,0.03)	0.07	-0.4 (-1,0.1)	0.1
5-a-day portions[d]	-0.6 (-1,-0.1)	0.006	-0.3 (-0.8,0.1)	0.1	-0.02 (-0.4,0.3)	0.9	-0.09 (-0.6,0.4)	0.6	-0.3(-0.8,0.04)	0.07	-0.3(-0.9, 0.2)	0.2
Total FV[e](g/day)	-46 (-81,-11)	0.009	-37 (-75,0.1)	0.05	-4 (-33,24)	0.7	-7 (-45,30)	0.6	-38 (-69,-7)	0.01	-47(-92,-2)	0.03
Nutrients (mg/d)												
Vitamin C diet only	-6 (-18,5)	0.2	-2 (-15,10)	0.7	-5 (-17,6)	0.3	2 (-13,17)	0.7	-5 (-18,7)	0.4	-4 (-23,14)	0.6
Vitamin C *	4 (-21,31)	0.7	3 (-24,32)	0.7	-26 (-53,0.1)	0.04	-29 (-63,5)	0.1	-0.1(-23,23)	0.9	-0.4(-34,33)	0.9
Biomarkers (µmol/l)												
Vitamin C	-3(-9,2)	0.2	2 (-3,9)	0.4	0.06 (-6,5)	0.9	5(-2,12)	0.2	-4(-9,1)	0.1	2(-5,10)	0.5
Total carot[f]	-0.4 (-0.7,-0.1)	0.007	-0.2 (-0.5,0.1)	0.2	-0.2 (-0.4,-0.006)	0.04	-0.1 (-0.4,0.1)	0.2	-0.1(-0.3,0.09)	0.2	-0.08(-0.4,0.2)	0.5
α-carotene	-0.01 (-0.04,0.009)	0.2	-0.01 (-0.04,0.01)	0.4	-0.007 (-0.02, 0.01)	0.4	-0.004 (-0.03,0.02)	0.6	0.001(-0.01,0.02)	0.8	-0.01(-0.04,0.01)	0.3
β-carotene	-0.07 (-0.1, -0.03)	0.1	-0.01 (-0.1, 0.1)	0.7	-0.03 (-0.1,0.03)	0.3	0.04(-0.05,0.1)	0.3	-0.002(-0.06,0.05)	0.9	-0.04(-0.1,0.04)	0.3
Lycopene	-0.1 (-0.2,0.08)	0.2	-0.02(-0.2,0.1)	0.8	-0.02 (-0.1, 0.1)	0.7	-0.03 (-0.2, 0.1)	0.7	0.03(-0.1,0.2)	0.6	0.1(-0.1,0.3)	0.4

Legend: FV (fruits and vegetables), g (gram), l (litre), µmol (micromole), m (milligram), n (number), veg (vegetables).

Model 2 adjusted for age, sex, socio-economic status, smoking, ethnicity and food energy.

[a)] Total fruit (not including juice) = Fruit (g) +Dried fruit (g) + Smoothie fruit (g)
[b)] Total vegetables= Beans (g) + Brassicaceae (g) + Other Vegg + Tomatoes (g) + Tomato Puree (g) +Yellow Red Green (g).
[c)] FV portions= (Fruit (g) + Driedfruitx3_mean + Tompureex5 mean + beans max mean+ Brassicaceae (g) + Yellow Red Green (g) + Other veg (g) + Tomatoes (g)) / 80 .
[d)] 5-a-day portions (portions/day) = Fruit veg portions + Fruit juice portions+ Smoothie Fruit portions
[e)] Total FV (not including juice) = Total fruit +Total vegetables
[f)] Total carotenoids = Lutein + alpha-cryptoxanthin + beta-cryptoxanthin+ lycopene + alpha-carotene + beta-carotene
*Vitamin C including supplements

Appendix D.8. Longstanding illnesses included.

Cancer (neoplasm) including lumps, masses, tumours, and growths and benign (non-malignant) lumps and cysts.
Diabetes including hyperglycaemia.
Other endocrine/ metabolic.
Mental illness/anxiety/depression/nerves.
Mental handicap.
Epilepsy/fits/convulsions.
Migraine/ headaches.
Other problems of nervous system.
Cataract/ poor eye sight/ blindness.
Other eye complaints.
Poor hearing/deafness.
Tinnitus/noises in the ear.
Meniere's disease/ear complaints causing balance problems.
Other ear complaints.
Stroke/cerebral haemorrhage/cerebral thrombosis.
Heart attack/angina.
Hypertension/high blood pressure/blood pressure.
Other heart problems.
Piles/haemorrhoids including Varicose Veins in anus.
Varicose veins/phlebitis in lower extremities.
Other blood vessels/embolic.
Bronchitis/emphysema.
Asthma.
Hay fever.
Other respiratory complaints.
Stomach ulcer/ulcer/abdominal hernia/rupture.
Other digestive complaints (stomach, liver, pancreas, bile ducts, small intestine).
Complaints of bowel/colon (large intestine, caecum, bowel, colon, rectum).
Complaints of teeth/mouth/tongue.
Kidney complaints.
Urinary tract infection.
Other bladder problems/incontinence.
Reproductive system disorders.
Arthritis/rheumatism/fibrosis.
Back problems/slipped disc/spine/neck.
Other problems of bones/joints/muscles.
Infectious and parasitic disease.
Disorders of blood and blood forming organs and immunity disorders.
Skin complaints.
Other complaints.
Unclassifiable (no other codable complaint).
Complaint no longer present.

Appendix E: Supplementary information for Chapter 5

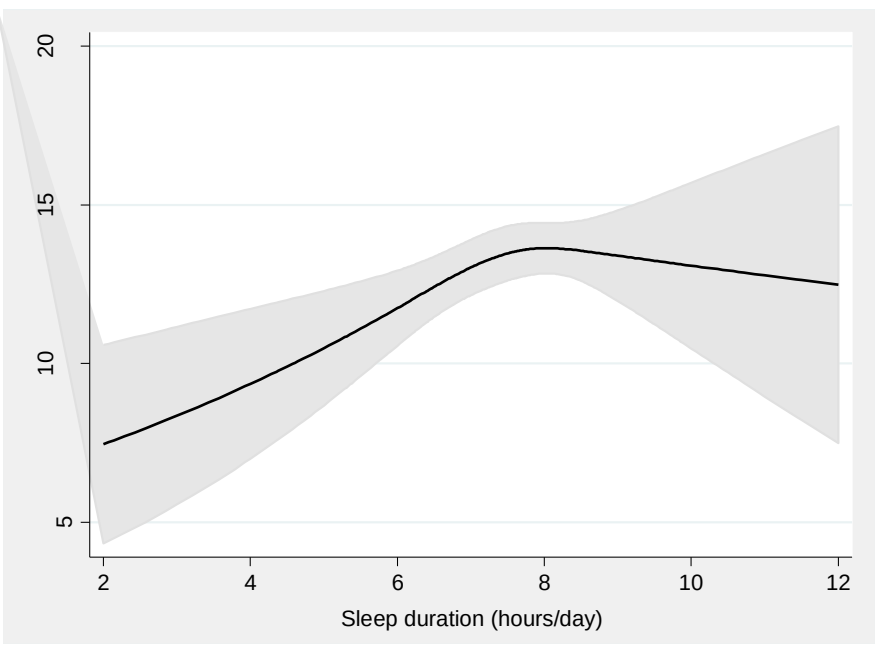
Appendix E.1. Characteristics' comparison between Phase 2 women and Snacking sub-study women from the UKWCS.

Sample **Characteristics**	**Phase 2*** **Mean (n)**	**Snacking sub-study** **Mean (n)**	 **P value****
Age (years)	52.5 (11,883)	51.4 (2,193)	<0.001
BMI (kg/m^2)	24.2 (11,420)	23.6 (2,105)	<0.001
Fruit (g/day)	225 (10,367)	265 (2,190)	<0.001
Vegetables (g/d)	215 (10,547)	234 (2,208)	<0.001
Total FV (g/d)	435 (10,557)	492 (2,209)	<0.001
Total energy intake (kcal/d)	2362 (11,944)	2363 (2,200)	0.9
	% (n)	**% (n)**	**P value****
Has longstanding illness (yes)	27 (3,240)	23 (513)	<0.001
Taking prescribed medicine (yes)	31 (3,630)	30 (622)	0.05
Smoking (yes)	9 (1,034)	7 (149)	0.003
Supplements (yes)	60 (6,514)	63 (1,262)	0.01
Vegetarian or vegan (yes)	29 (3,498)	47 (1,043)	<0.001
Ethnicity (white)	99 (11,553)	99 (2,133)	0.3
Employer (employed)	58 (7,003)	62 (1,366)	0.001
Socio-economic status (professional)	27 (3,225)	30 (667)	0.04
Physical activity (light/ moderate)	50 (5,639)	47 (996)	<0.001
Marital status (married)	76 (9,006)	76 (1,647)	0.2
Number of children (2 children)	51 (4,729)	50 (817)	0.4

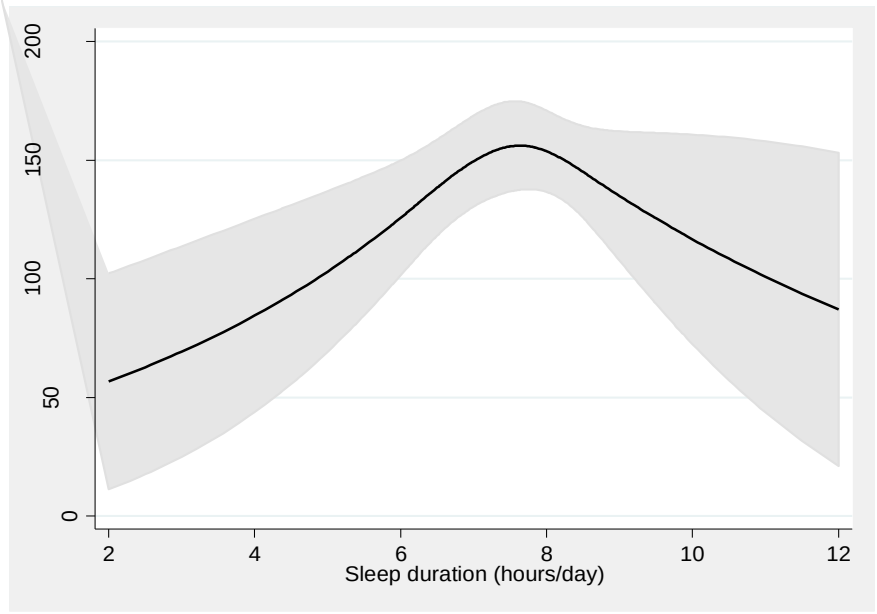
Legend: BMI (body mass index), d (day), FV (fruits and vegetables), g (gram), n (number).
*Excluding women from the Snacking sub-study
**One-way analyses of variance (ANOVA) was conducted to obtain p value between Phase 2 and Snacking sub-study women in continuous variables and chi square test was used for categorical variables

Appendix E.2. The associations between sleep duration and fruit and vegetable biomarkers from the restricted cubic spline modelling. Black lines plot the predicted FV biomarkers values E.2.1) vitamin C E.2.2) α-carotene E.2.3) β-carotene E.2.4) lycopene with 95% confidence interval (grey shaded area) for typical women from the UKWCS (white, non-smokers, professional status).

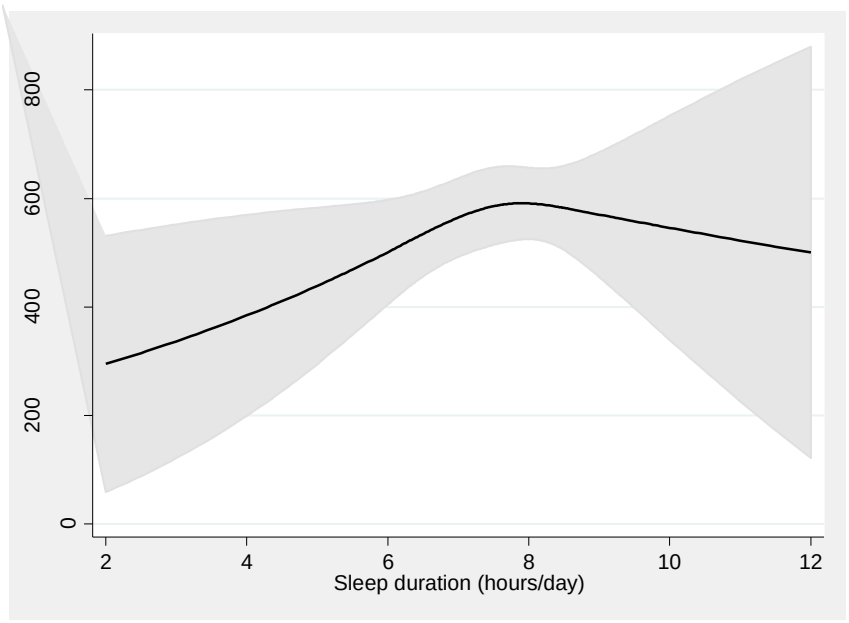
E.2.1 Vitamin C, non-linear (p=0.02)



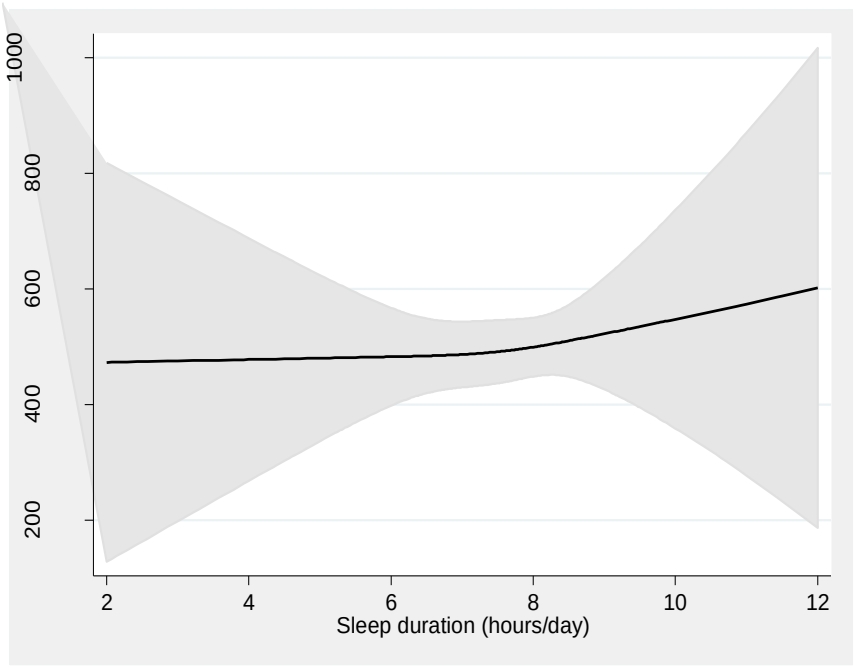
E.2.2 α-carotene, non-linear (p=0.05)



E.2.3 β-carotene, linear (p=0.2)



E.2.4 Lycopene, linear (p=0.8)



Appendix E.3. Association between sleep duration categories and fruit and vegetable intakes after excluding supplement users from the UKWCS.

Short sleepers (≤6 h/d) and long sleepers (≥9 h/d) compared to the recommended group (7-9 h/d)						
	Model 2					
Sleep categories	**≤ 6 h/d sleep**		**≥9 h/d sleep**			
FV (g/d)**	**Mean difference (95% CI)**	**P value**	**Mean difference (95% CI)**	**P value**	**n**	**Overall P value***
Fruit	-3 (-17, 11)	0.6	-14 (-28, -0.5)	0.04	5,199	0.1
Vegetables	-7 (-17, 3)	0.1	-21 (-31,-10)	<0.001	5,284	<0.001
Total FV	-16 (-36,3)	0.1	-33 (-53,-14)	0.001	5,293	0.001
FV (serving/week)***						
Fruit	-0.2 (-0.8 ,0.4)	0.4	-1 (-1, -0.5)	<0.001	5,909	0.001
Vegetables	-0.1 (-0.7, 0.5)	0.6	-0.8 (-1,-0.1)	0.01	5,936	0.04
Total FV	-0.4 (-1, 0.6)	0.4	-1 (-3, -0.9)	<0.001	5,982	<0.001

Legend: d (day), FV (fruits and vegetables), g (gram), h (hour), n (number).

7,776 participants who reported the consumption of vitamins, minerals or/and food supplements were excluded

Model 2 adjusted for age, socio-economic status, smoking, ethnicity and total calories

* P value for differences between sleep duration categories

** obtained from 4-day food diary

*** obtained from health and lifestyle questionnaire

Appendix E.4. Association between sleep duration categories and fruit and vegetable intakes after excluding vegan or/and vegetarian women from the UKWCS.

Short sleepers (≤6 h/d) and long sleepers (≥9 h/d) compared to the recommended group (7-9 h/d)						
Model 2						
Sleep categories	**≤ 6 h/d sleep**		**≥9 h/d sleep**			
FV (g/d)**	**Mean difference (95% CI)**	**P value**	**Mean difference (95% CI)**	**P value**	**n**	**Overall P value***
Fruit	-4 (-15, 6)	0.4	-12 (-23,-1)	0.02	7,871	0.06
Vegetables	-10 (-18, -2)	0.008	-10 (-18,-3)	0.007	7,994	0.001
Total FV	-17 (-32,-2)	0.02	-24 (-39,-9)	0.001	8,007	<0.001
FV(serving/week)***						
Fruit	-0.5 (-1 ,-0.08)	0.02	-0.9 (-1, -0.4)	0.001	8,940	<0.001
Vegetables	-0.5 (-1,-0.1)	0.01	-0.3 (-0.8,0.1)	0.1	8,964	0.03
Total FV	-1 (-2,-0.4)	0.002	-1 (-2, -0.4)	0.002	9,023	<0.001

Legend: d (day), FV (fruits and vegetables), g (gram), h (hour), n (number).

4,541 participants that reported being vegan/vegetarian were excluded

Model 2 adjusted for age, socio-economic status, smoking, ethnicity and total calories

* P value for differences between sleep duration categories

** obtained from 4-day food diary

*** obtained from health and lifestyle questionnaire

Appendix E.5. Association between sleep duration categories and fruit and vegetable intakes after excluding women with a longstanding illness from the UKWCS.

Short sleepers (≤6 h/d) and long sleepers (≥9 h/d) compared to the recommended group (7-9 h/d)						
	Model 2					
Sleep categories	**≤6 h/d sleep**		**≥9 h/d sleep**			
FV (g/d)**	**Mean difference (95% CI)**	**P value**	**Mean difference (95% CI)**	**P value**	**n**	**Overall P value***
Fruit	-8 (-20, 4)	0.1	-14 (-26,-2)	0.02	8,528	0.04
Vegetables	-7 (-16, 1)	0.1	-11 (-20,-2)	0.009	8,652	0.01
Total FV	-18 (-34,-1)	0.02	-25 (-41,-9)	0.002	8,657	0.001
FV(serving/week)***						
Fruit	-0.5 (-1 ,-0.04)	0.03	-0.9 (-1, -0.4)	0.001	9,692	<0.001
Vegetables	-0.1 (-0.6, 0.3)	0.5	-0.4 (-0.9,0.09)	0.1	9,712	0.2
Total FV	-0.7 (-1,0.08)	0.07	-1 (-2,-0.6)	0.001	9,790	0.001

Legend: d (day), FV (fruits and vegetables), g (gram), h (hour), n (number).

3,753 participants that reported having a longstanding illness were excluded

Model 2 adjusted for age, socio-economic status, smoking, ethnicity and total calories

* P value for differences between sleep duration categories

** obtained from 4-day food diary

*** obtained from health and lifestyle questionnaire

Appendix E.6. Association between sleep duration categories and fruit and vegetable intakes after excluding women consuming prescribed medicines from the UKWCS.

Short sleepers (≤6 h/d) and long sleepers (≥9 h/d) compared to the recommended group (7-9 h/d)						
Model 2						
Sleep categories	**≤6 h/d sleep**		**≥9 h/d sleep**			
FV (g/d)**	**Mean difference (95% CI)**	**P value**	**Mean difference (95% CI)**	**P value**	**n**	**Overall P value***
Fruit	-1 (-13,11)	0.8	-8 (-21, 4)	0.1	8,108	0.4
Vegetables	-6 (-15, 2)	0.1	-10 (-19,-0.8)	0.03	8,216	0.05
Total FV	-10 (-26,6)	0.2	-17 (-34,-0.3)	0.04	8,220	0.08
FV(serving/week)***						
Fruit	-0.2 (-0.7 ,0.3)	0.3	-0.9 (-1, -0.3)	0.003	9,189	0.009
Vegetables	-0.1 (-0.7, 0.3)	0.5	-0.3 (-0.8,0.2)	0.2	9,220	0.4
Total FV	-0.4 (-1, 0.4)	0.3	-1 (-2, -0.4)	0.004	9,284	0.01

Legend: d (day), FV (fruits and vegetables), g (gram), h (hour), n (number).

4,252 participants that reported having long term treatment for illness were excluded

Model 2 adjusted for age, socio-economic status, smoking, ethnicity and total calories

* P value for differences between sleep duration categories

** obtained from 4-day food diary

*** obtained from health and lifestyle questionnaire

Appendix E.7. Association between sleep duration categories and fruit and vegetable intakes, including body mass index as an adjustment in women from the UKWCS.

Short sleepers (≤6 h/d) and long sleepers (≥9 h/d) compared to the recommended group (7-9 h/d)						
	Model 2 (including BMI)					
Sleep categories	**≤6 h/d sleep**		**≥9 h/d sleep**			
FV (g/d)**	**Mean difference (95% CI)**	**P value**	**Mean difference (95% CI)**	**P value**	**n**	**Overall P value***
Fruit	-3 (-13,6)	0.4	-11 (-22 -1)	0.02	11,108	0.06
Vegetables	-8 (-15,-1)	0.02	-9 (-16, -2)	0.01	11,264	0.004
Total FV	-14 (-28,-1)	0.03	-21 (-34,-7)	0.002	11,275	0.001
FV(serving/week)***						
Fruit	-0.5 (-0.9,-0.08)	0.01	-1 (-1, -0.5)	<0.001	12,564	<0.001
Vegetables	-0.3 (-0.7, 0.1)	0.1	-0.2 (-0.7, 0.1)	0.2	12,600	0.2
Total FV	-0.8 (-1, -0.1)	0.01	-1 (-2, -0.5)	<0.001	12,689	<0.001

Legend: BMI (body mass index), d (day), FV (fruits and vegetables), g (gram), h (hour), n (number).

Participants with a body mass index <18 and >50 kg/m^2 were excluded from the analyses (n= 208)

Model 2 adjusted for age, socio-economic status, smoking, ethnicity and total calories (including BMI in this analyses)

* P value for differences between sleep duration categories

** obtained from 4-day food diary

*** obtained from health and lifestyle questionnaire

Appendix E.8. Association between weekday/weekend sleep duration categories and fruit and vegetable intakes of women from the UKWCS.

Short sleepers (≤6 h/d) and long sleepers (≥9 h/d) compared to the recommended group (7-9 h/d)						
Model 2						
Weekday sleep categories	**≤6 h/d sleep**		**≥9 h/d sleep**			
FV(g/d)**	**Mean difference (95% CI)**	**P value**	**Mean difference (95% CI)**	**P value**	**n**	**Overall P value***
Fruit	-4 (-13 ,4)	0.3	-18 (-23, -8)	<0.001	11,256	<0.001
Vegetables	-5 (-12 ,0.7)	0.08	-10 (-18,-3)	0.003	11,417	0.005
Total FV	-13 (-25,-0.9)	0.03	-29 (-42 ,-16)	<0.001	11,428	<0.001
FV(serving/week)***						
Fruit	-0.1(-0.5,0.3)	0.6	-1 (-1,-0.7)	<0.001	12,762	<0.001
Vegetables	-0.2(-0.6,0.1)	0.2	-0.5 (-1,-0.1)	0.01	12,800	0.02
Total FV	-0.4 (-1 ,0.2)	0.2	-1 (-2,-1)	<0.001	12,892	<0.001
Weekend sleep categories	**≤6 h/d sleep**		**≥9 h/d sleep**			
FV (g/d)**	**Mean difference (95%CI)**	**P value**	**Mean difference (95%CI)**	**P value**	**n**	**Overall P value***
Fruit	-3 (-14 ,7)	0.5	-16 (-23 ,-9)	<0.001	11,138	<0.001
Vegetables	-6 (-14, 1)	0.1	-9 (-14 ,-4)	<0.001	11,294	<0.001
Total FV	-12 (-26 ,1)	0.08	-26 (-36,-17)	<0.001	11,304	<0.001
FV (serving/week)***						
Fruit	-0.3(-0.8,0.1)	0.1	-0.9 (-1,-0.6)	<0.001	12,597	<0.001
Vegetables	-0.2(-0.7,0.1)	0.2	-0.5 (-0.8 ,-0.2)	<0.001	12,635	0.001
Total FV	-0.6 (-1,0.1)	0.09	-1 (-2 ,-1)	<0.001	12,728	<0.001

Legend: d (day), FV (fruits and vegetables), g (gram), h (hour), n (number).

Model 2 adjusted for age, socio-economic status, smoking, ethnicity and total calories
* P value for differences between sleep duration categories
** obtained from 4-day food diary
*** obtained from health and lifestyle questionnaire